



# SURGERY

## Gynecology and Obstetrics

An International Journal of Surgery

FRANKLIN H. MARTIN, M.D.

*Founder and Managing Editor 1905-1935*

Volume 76

JANUARY TO JUNE, 1943

PUBLISHED BY

THE SURGICAL PUBLISHING COMPANY OF CHICAGO

54 EAST ERIE STREET, CHICAGO, ILLINOIS, U.S.A.

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# SURGERY

## GYNECOLOGY AND OBSTETRICS

*An International Magazine, Published Monthly*

VOLUME 76

JANUARY, 1943

NUMBER I

### INJURIES OF THE PARIETES AND EXTREMITIES

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MANY men have made helpful contributions toward solving the problems involved in the treatment of wounds and compound injuries. With all deference to the legion of surgeons whose efforts have culminated in the methods of treatment in use today four men should be mentioned—one no longer living—whose writings deserve careful reading by every surgeon interested in the treatment of wounds. Those men are Hugh Owen Thomas (of the Thomas splint), H. Winnett Orr, Mont Reid, and Vilray P. Blair. Their contributions, needless to say, are concerned particularly with surgical principles rather than with exact details of technique.

One of the primary principles that guided Thomas in his treatment of wounds and injuries is epitomized in his oft repeated dictum, "Inflamed and injured tissues need rest," a principle oft forgotten, but rediscovered during the past few years and emphasized so often and so forcibly that it should never again be relegated to a secondary place in surgical teaching. Orr, and subsequently Trueta, reaffirmed this principle.<sup>1</sup> Orr demonstrated its importance particularly in the care of patients with chronic and persistent in-

fection of bone. He demonstrated a second principle, which his kindness and consideration for his professional colleagues did not permit him to emphasize, namely, that nature unhindered can often accomplish more for the patient with a compound fracture or a chronic osteomyelitis than the unthinking surgeon who repeatedly tears down healing tissue and constantly adds infection to an open wound as he dresses it with careless hands, and breathes and talks over it with unmasked nose and uncovered mouth, perhaps when the very atmosphere is harboring virulent bacteria. If such a statement sounds harsh to the reader's ear he has only to read some of the comments that have come from overseas in the past 12 months to realize that much harsher things have been said.<sup>2</sup>

Blair's paper on the helpful effect of pressure on wound healing also represents a principle which in Homans' words has been "perennially discovered, discredited, forgotten, rediscovered and reaffirmed." In spite of the repeated emphasis of Blair and many others on the importance of pressure in preventing congestion and helping to maintain the circulation in the subcutaneous tissues, in spite of the fact that almost every layman knows that the simplest way to stop bleeding,

cesses while ignoring the obvious fact that the chief purpose of a plaster cast is to confer absolute rest on an injured part but that it can do so only if it is adequate in size, correctly designed and well applied." (Lancet, 1940 2:45)

<sup>2</sup>"Often (hospital) infection occurs in the already infected wound. Sepsis is piled upon sepsis, etc."

From the Division of Surgery, Northwestern University Medical School.

<sup>1</sup>In spite of Dr. Trueta's careful instructions, many surgeons seem to feel that a white crust round a dressing casts a magic spell over the wound; it encloses, they will discuss the supposed action of the bacteriophage and of calcium ions in healing pro-



whether from an open wound or from subcutaneous trauma, is by the application of moderate pressure, only after continued use had repeatedly demonstrated its value in the treatment of compound fractures of the long bones was it generally recognized that the smooth uniform pressure of a plaster cast was an important factor in preventing exudation into the injured tissues and in helping to maintain an adequate circulation. That the same pressure can be advantageously applied, whether with plaster or some other form of pressure dressing, whenever there has been an injury of the soft tissues alone and that it is of greatest value where the injury is of great extent, as in the case of a severe burn, has often been demonstrated but too often before unseeing eyes.

Reid's paper "Some Considerations of the Problems of Wound Healing," could well be required reading for every surgeon who has the obligation and opportunity of treating patients with open wounds. It is a thoughtful, comprehensive and wholly admirable discussion of the factors at work and the principles involved in wound repair.

THE principles involved in the care of wounds of the parietes and extremities do not differ from those applicable to all wounds. Primary considerations are (1) arrest of hemorrhage and treatment of shock, (2) prevention of additional contamination and trauma, (3) diagnosis of the extent of injury, (4) conversion of the contaminated wound into a clean wound if the time interval still permits, (5) removal of foreign material and devitalized tissue, (6) repair of injured structures, (7) purposeful dressing and splinting to provide rest and an adequate circulation for injured tissues, whether bone or soft tissues, (8) cleanly surgical care until healing is complete. Under conditions of stress and when suddenly confronted with many seriously injured patients the surgeon cannot carry out the treatment suggested in the paragraphs immediately following. In subsequent paragraphs methods of treatment to be adopted in emergencies are outlined. Unless, however, the surgeon keeps clearly in mind the basic surgical principles that under-

lie successful treatment he can easily fail to accomplish satisfactory results, no matter what conditions obtain.

#### 1. ARREST OF HEMORRHAGE AND TREATMENT OF SHOCK

It is often forgotten that simple pressure will stop bleeding in the majority of cases if the pressure is applied in the right place. Digital pressure over a few pads of sterile gauze is more likely to be effective than a massive gauze dressing held with a circular bandage. A spurting vessel can be caught with a sterile hemostat and the forceps included in the covering dressing. The hasty effort to arrest bleeding with ungloved hands and incompletely sterilized instruments may lead to further and serious wound contamination. If a constrictor must be used the inflated blood pressure cuff is least likely to lead to compression injury of nerves and soft tissues.

"Elevation of the bleeding wound is of importance. If it can be done without too much manipulation. In our dispensary we see many people come in with bleeding wounds and improperly applied tourniquets. Removal of the tourniquet and simple elevation of the part stop the bleeding" (Reid).

The necessity for recognition and treatment of shock needs no emphasis. Many a surgeon has learned from bitter experiences the disastrous results that can follow operation on the pale, severely injured patient "with a rapid pulse and cold nose. The importance of the subject has been stressed by every writer concerned with the treatment of wounds. In the surgical emergencies of today patients with impending or actual shock should receive more skillful and efficient treatment than it has ever been possible to achieve in the past.

#### 2. PREVENTION OF ADDITIONAL CONTAMINATION AND TRAUMA

The most feared sources of added contamination of open wounds are the uncovered noses and mouths of first aid workers and of all others who share in the subsequent care of the patient. The ungloved hands of those who are constantly working with patients with contaminated wounds, incompletely sterilized instruments and surgical supplies

dust borne infection in wards or dressing rooms constantly used in the care of patients with infected wounds<sup>1</sup> The most common forms of trauma superimposed on the initial injury are the chemical trauma of powerful antiseptics, the mechanical trauma of probing and "investigation" of the wound, and the trauma that results from constant movement of unsupported and unsplinted fractured tissues

How can these be reduced to a minimum? First, and of very great importance, by having all personnel working with patients with open wounds capped and masked Second, by covering the open wound at the earliest possible moment with an occlusive sterile dressing bandaged in place with moderate pressure and left undisturbed until adequate surgical care can be given and under the most favorable conditions available Third, by avoiding the addition of tincture of iodine and other so-called antiseptics that fix, coagulate, and destroy living tissues, and that are particularly damaging to the delicate tissues underneath the skin which are ill adapted to resist such injury<sup>2</sup> Fourth, by avoiding any probing or examination of the open wound Fifth, by immobilizing the injured part as completely as possible and at the earliest possible moment by the simplest method available that provides rest for the injured tissues and uniform pressure over the affected area

## 3 DIAGNOSIS OF THE EXTENT OF INJURY

It is easy to forget that diagnosis should precede treatment when one is dealing with patients with open wounds and under unusual and trying conditions *An estimate of the patient's general condition and recognition of the presence of multiple injuries and unusual injuries are of primary importance* The tiny

<sup>1</sup>The admirable papers of Hare and the reports of Colebrook and Fleming have stressed the importance of human sources of contamination and the incriminating evidence yielded by repeated examination of the bacteriological flora of open wounds.

<sup>2</sup>Today with our knowledge of the delicacy of growing living cells and of their lethal susceptibility to alcohol, ether, iodine, mercurochrome, merthiolate, carbolic acid, bichloride of mercury, and countless other substances people go blithely on pouring them into open fresh wounds to kill living cells and to complicate the process of wound healing and to promote the chances of infection So far as fresh traumatic wounds are concerned we would today be far better off with a total ignorance of all chemical bactericidal agents and if we only utilized our knowledge of bacteria and of wound healing by gentle mechanical cleaning of the surrounding skin and open wound of all dirt, foreign bodies, dead or devitalized tissue and by flooding the invisible bacteria away by means of sterile salt solution (Reid Mont R N England J M, 1936 215 753-765)

wound of the buttock that marks the site of entry of a shell splinter that has perforated a viscus, the scratch of the lumbar region at the point of entry of a metal fragment that has perforated the colon, the bleeding wound of an extremity that diverts attention from a compression of the spine are only a few of the many "traps" that can be avoided by unrelenting watchfulness and care

Injuries of the extremities lend themselves particularly to diagnosis of the extent of local injury because of the signs that can usually be elicited distal to the site of injury One must consider in turn blood vessels, bones, nerves, and tendons

Injuries of blood vessels are evidenced by the obvious signs of hemorrhage, by the pallor or cyanosis of all the extremities when the blood escapes, and by the increasing swelling, tension, and discoloration of the affected limb that accompany concealed hemorrhage The absence of radial or tibial pulse and the lowered temperature of the limb are significant and easily elicited signs of severe obvious or concealed vascular injury Combined arteriovenous injuries are not uncommon as a result of deep penetrating wounds

Injuries of bone are not likely to be overlooked because of the obvious loss of function invariably present In cases of doubt it is wise to assume that some bone injury is present The exact information that can be obtained from x-ray examination is often invaluable

Injuries of nerves are usually easy to recognize and are of all injuries most often overlooked The motor and sensory signs of median, ulnar, and radial nerve injury in the upper extremity, and of tibial and peroneal injury in the lower are clear cut, easy to elicit, and within a period of from 3 to 6 hours after injury are not misleading Later, edema and swelling may cause pressure upon nerve fibers and give signs of division when only compression is present In Figures 1 to 6 are indicated methods of recognizing the most common and important nerve injuries involving the upper extremities With reference to the lower extremities it is important to remember that sensation over the anterior and lateral aspect of the leg and dorsum of the foot is controlled

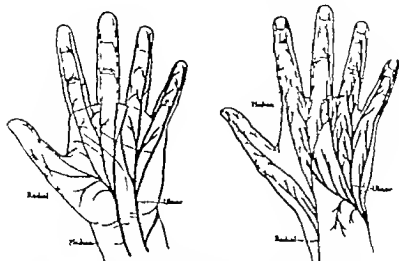


Fig. left. The sensory nerve supply of the palm (after Spalteholz)

Fig. r. The sensory nerve supply of the dorsum of the hand (after Spalteholz).

by the common peroneal nerve over the medial and posterior aspect of the leg and plantar surface of the foot by the tibial nerve.

Dorsal flexion at the ankle and extension of the toes are controlled by the common peroneal extension at the ankle joint and flexion of the toes by the tibial nerve

Tendon injuries can be recognized as definitely as nerve injuries. The diagnosis requires a few minutes of time and accurate anatomical knowledge (Figs. 5-6)

#### 4. CONVERSION OF THE CONTAMINATED WOUND INTO A CLEAN WOUND

Surgeons are not all in agreement as to the best method. Theoretically if one could cleanse the area about the wound, and carry out complete excision of contaminated tissue without permitting the knife to come in contact with the contaminated surface of the open wound, he would rid the patient of all contaminated tissue "at one stroke" (Figs. 7-8). Practically such a procedure is difficult to carry out even with great care and in the case of a superficial wound. It is almost impossible to accomplish in the treatment of most wounds because wound tracts are irregular often tortuous in direction and surprisingly deep and

because one cannot sacrifice essential structures in order to accomplish complete excision of a contaminated wound. While complete excision may be applicable in the case of very superficial wounds, or wounds in which subcutaneous tissue and muscle alone are involved the surgeon who attempts to apply the principle of complete excision to all wounds finds himself at a loss when he is confronted with tendons, nerves, blood vessels and perhaps bone fragments and open joint cavities exposed to the same contamination which he has been attempting to remove by a complete excision.

In our judgment the most certain and practical method of converting every type of contaminated wound into a clean wound is first of all to wash the area around the wound and then the wound itself thoroughly patiently and gently with plain white soap and water applied with soft cotton and with hands covered with sterile gloves (Fig. 9) and secondly to irrigate the wound with sterile salt solution. While the area about the wound is cleansed the wound itself is protected with the inner portion of the occlusive dressing originally applied. When the surrounding area is cleansed the dressing is removed and the wound itself cleansed in the same way. If the

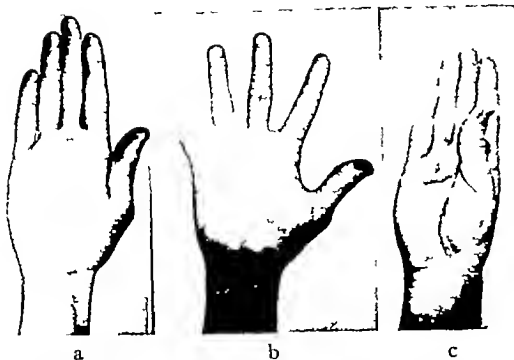


Fig 3 a, Adduction of the fingers toward the middle finger, b, abduction of the fingers from the middle finger, and c, adduction of the thumb toward the hand are carried out by the interossei, the muscles of the hypothenar eminence and the adductor pollicis, all of which are supplied by the ulnar nerve

wound is clean cut, incised and with little evidence of contamination no effort is made to wash the wound surface with soapy solution, but we believe no harm is done if the solution comes in contact with it. The more jagged and irregular the wound the more careful and prolonged the cleansing, if necessary wound edges are held apart with retractors, and if indicated the cleansing solution and the gloves of the operator are changed during the cleansing procedure. Finally, every recess of the wound is thoroughly irrigated with warm sterile salt solution.

Why this particular method? Because it is simple, because it requires only patience and care, and not unusual surgical ability, because it is applicable to every type of injury, because it works.

As evidence of the successful results that can be obtained by such a method and of the fact that the theoretical danger of spreading contamination by cleansing wound surfaces is of little practical importance I would cite the following facts. Drs. Michael Mason, Harvey Allen, and I have carried out this method in the treatment of all open wounds which have come under our care during the past five years. Some of them have been extensive and comparable to the serious injuries seen in war (Figs 10 to 12). In only 3 of 103 cases with extensive injuries in which the patient came within 2 hours of the time of injury, in which first aid care had been limited

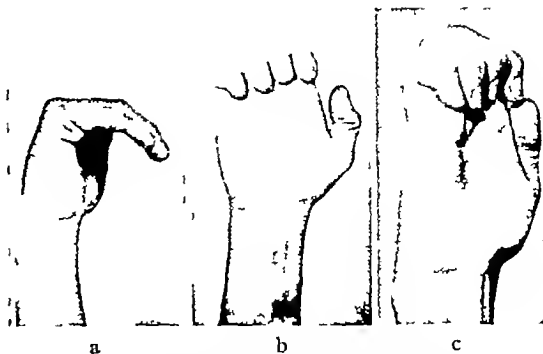


Fig 4 a, Flexion at the metacarpophalangeal joints is produced by the lumbricals and interossei. b, c, With injury or division of the median and ulnar nerves below the middle of the forearm the power of flexion at the metacarpophalangeal joints is lost, the fingers can still be flexed at the interphalangeal joints by the long flexor tendons

to the application of a pressure bandage and a sterile dressing, and in which the covering tissues could be approximated or completely replaced was there failure of primary union. Secondly, only since this method of treatment has been introduced at the Cook County Hospital have we consistently seen patients return to the Hand Clinic with primary healing after repair of open wounds with division of nerves and tendons. Thirdly, surgeons who are handling large numbers of cases of compound

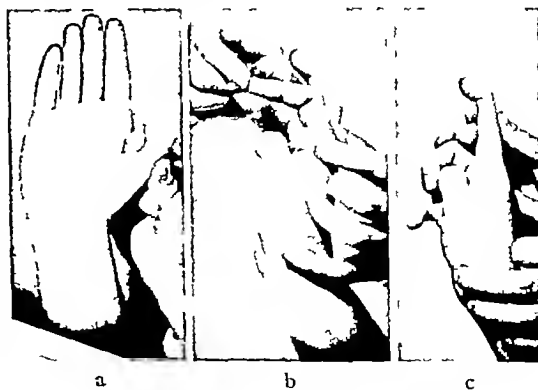


Fig 5 a, If the proximal phalanx of the thumb is held fixed active flexion at the interphalangeal joint is due solely to the action of the flexor pollicis longus. If the muscle or tendon is injured or divided, flexion is limited or the thumb remains fixed in extension. b, Position of the finger after division of the flexor profundus, active flexion at the proximal interphalangeal joint is produced by the flexor sublimis but the finger remains extended at the distal interphalangeal joint. c, If the flexor profundus is intact the finger can be flexed at the distal interphalangeal joint.

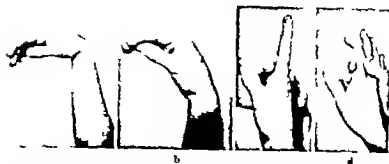


Fig. 6. a, Drop wrist of musculospiral or radial nerve injury. b, Loss of power of extension of the fingers due to laceration of the extensor carpi ulnaris tendon. c, With the proximal phalanges flexed or supported the fingers can be extended by the action of the humerocarpal and interosseous even though the extensor carpi ulnaris is divided. d, Loss of power of extension at the distal interphalangeal joint, due to division of the extensor tendon opposite the joint or avulsion of the tendon from its insertion on the distal phalanx.

Injuries are obtaining similarly consistent results.

The study of 36 injuries resulting in 244 compound wounds, revealed that hospitalization was necessary in 8 cases in which the primary care consisted of only soap and water cleansing and excision of only devitalized tissue. Seventy-five per cent of these compound injuries involved the wrist and hand. Of these 9, 05 cases only 1 patient required hospitalization. Because these injuries are so uniformly contaminated and so difficult of cleansing, and further because no instance which required primary soap and water cleansing as given, was it necessary to hospitalize an individual for infection. I feel that this is the severest test for the efficacy of the method. It is likewise seen that it is successful in the hands of the nurses. No care for the great majority of the minor compound wounds. In cases of compound fractures, there are 4 infections and in no instance osteomyelitis or delayed union from infection. (Kerrigan)

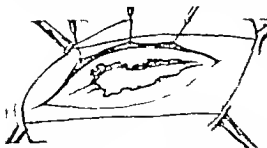


Fig. 7. The skin has been painted with skin antiseptic up to the wound edges and draped. No skin antiseptic and no alcohol, ether or soap has been allowed to enter the wound. The excision of the wound has been started. (Reed and Carter. See Surg. 427-49.)

#### 5. REMOVAL OF FOREIGN MATERIAL AND DEVITALIZED TISSUE

After wound cleansing is completed removal of any foreign bodies that remain and complete excision of devitalized tissue are carried out. If the contaminated wound has been transformed into a clean wound by careful cleansing the surgeon works at a great advantage. He is not tempted to sacrifice tissue ruthlessly to assure complete removal of possible contamination and it has been our observation that the effect of irrigation on injured tissues often helps him to differentiate devitalized tissue from living tissue.

What is devitalized tissue and how can it be recognized? Skin that is dead white, grayish-white or purple that does not bleed when cut nor change in color when gentle pressure is applied with a warm moist pack, muscle that is gray or reddish-gray and that does not contract when gently pinched, tendons and nerves that are discolored with blood, contused, and fragmented bone that is detached from muscle and periosteum—all these have little or no chance of survival furnish excellent media for bacterial growth and jeopardize wound healing.

The importance of excising completely tissue which is devitalized should not lead the surgeon into the error of sacrificing tissue which can be preserved. It is particularly important that skin should not be sacrificed

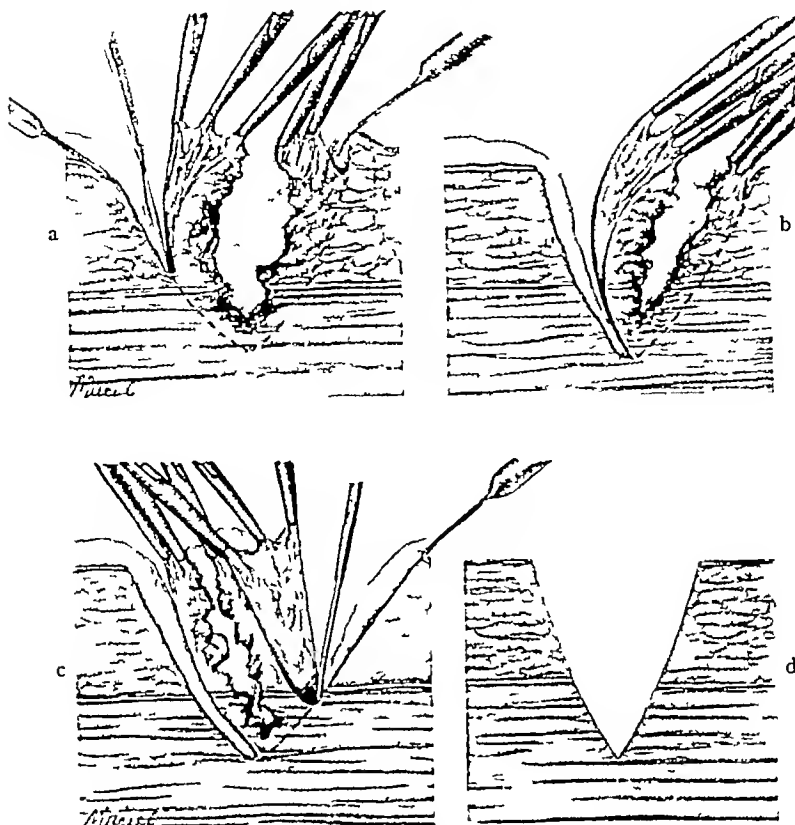


Fig 8 a, Hemostats have been applied to the skin edge which is to be excised. The excision has been carried down to the muscle. Fresh pads moistened with saline have been advanced down the clean side of the wound as the incision is deepened. b, The excision has been completed on one side. Note the protection by the gauze pad. c, The excision has been nearly completed. d, The completed excision. The wound is now irrigated copiously with normal salt solution and fresh drapings are applied. (Reid and Carter, *Ann Surg*, 1941, 114: 10)

needlessly, for of all tissues it is the most viable and most necessary" (*Lancet*, 1940, 2: 46). The needless sacrifice of bone fragments still attached to muscle and periosteum and the subsequent failure of the fractured bone to unite were often commented upon during the last war. As Mr. Anderson has emphasized, excision of devitalized tissue should begin at the proximal end of the wound so as to avoid leaving behind tissue with impaired blood supply as tissues farther proximalward are excised.

#### 6 REPAIR OF INJURED STRUCTURES

How far one should go toward repair of injured structures depends first of all upon

whether one can reasonably expect healing by primary union. The character of the first aid treatment that has been given, the time that has elapsed since the injury, the character and extent of the wound, the condition of the patient, the time and facilities available for repair must all be taken into consideration.

The way in which first aid treatment has been given is of great importance. The danger of inoculating the open wound with virulent organisms from the mouth and nose of unmasked first aid workers has been stressed above. So much importance do we attach to this potential source of infection that we are unwilling to consider wound repair and closure



Fig. 9. Preparation of the field of operation: a, A small table with a basin of sterile cotton, cake of plaster, hot soap, towel and dry sterile gloves, is ready beside the operating table; b, Cleansing of the field of operation is gentle, but thorough and painstaking, and is continued for at least 30 minutes.

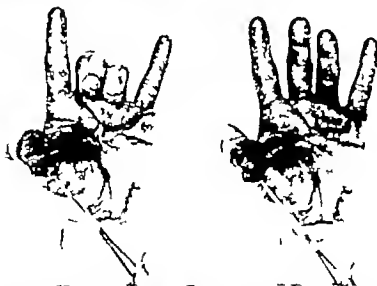


Fig. 10. Lacerated wound of hand with division of extensor pollicis longus and brevis, abductor pollicis longus, thenar muscles, capsule of metacarpophalangeal joint of thumb, both digital nerves of thumb, flexor tendons of index finger, and digital nerve on radial side and flexor tendons and both digital nerves of little finger. The thumb is attached to the hand only by pedicle of skin and subcutaneous tissues in the web. Immediate soap and water cleansing, repair of divided structures and closure of wound without drainage. Primary union. (Patient of Dr. Michael Mason. *West J Surg* 9:57-45-247.)



Fig 11 Result 3 months after repair of injury shown in Figure 10 (Patient of Dr Michael Mason *West J Surg*, 1937, 45 248)

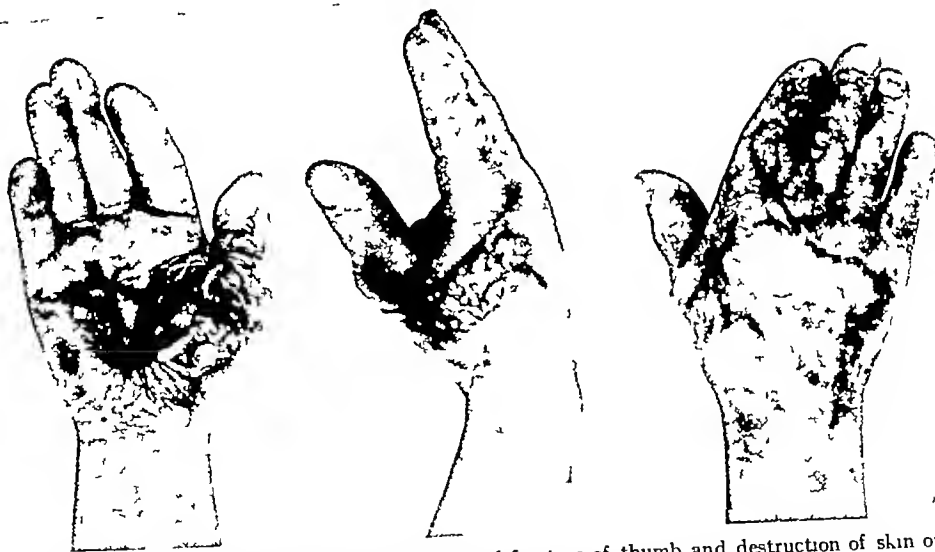


Fig 12 Crushing injury of hand with compound fracture of thumb and destruction of skin over dorsal surface of middle and distal phalanges of index finger. Immediate cleansing of wound and primary closure with sutures and skin graft (Patient of Dr Michael Mason *Indust M*, 1941, 10 48)

if bleeding vessels have been tied and any effort made to "disinfect the wound" under conditions of which we cannot know. Time and again we have seen extensive wounds heal by primary union when the first aid care was limited to the application of a sterile dressing, and subsequent care given under favorable conditions (Figs 10 to 14). On the other hand the few serious infections we have encountered

as a complication of open wounds have developed in patients who were first treated in hospitals or offices which specialized in "Emergency Surgery, 24 hour service," where the use of masks was the exception rather than the rule, and where the surgeon relied chiefly upon antiseptics and upon sulfonamides in order to combat potential or already developed infection.





Fig. 3. Appearance of hand shown in Figure 1 at primary dressing weeks after injury and 3 months after injury (Patient of Dr. Michael Simon, Indust. M. 94)

The time that has elapsed following the injury is an important consideration. Although some surgeons consider that it is permissible to close an open wound at any time

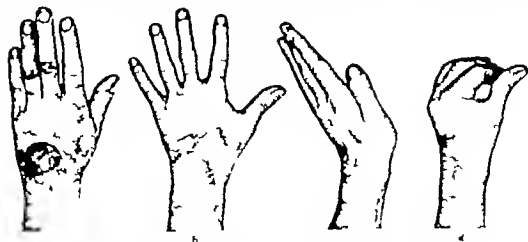


Fig. 4. Cracking lateral end of hand with division of extensor tendons of middle and ring fingers. Immediate repair and after cleansing suture of tendons and repair of wound. b. Functional result weeks after repair of injury.

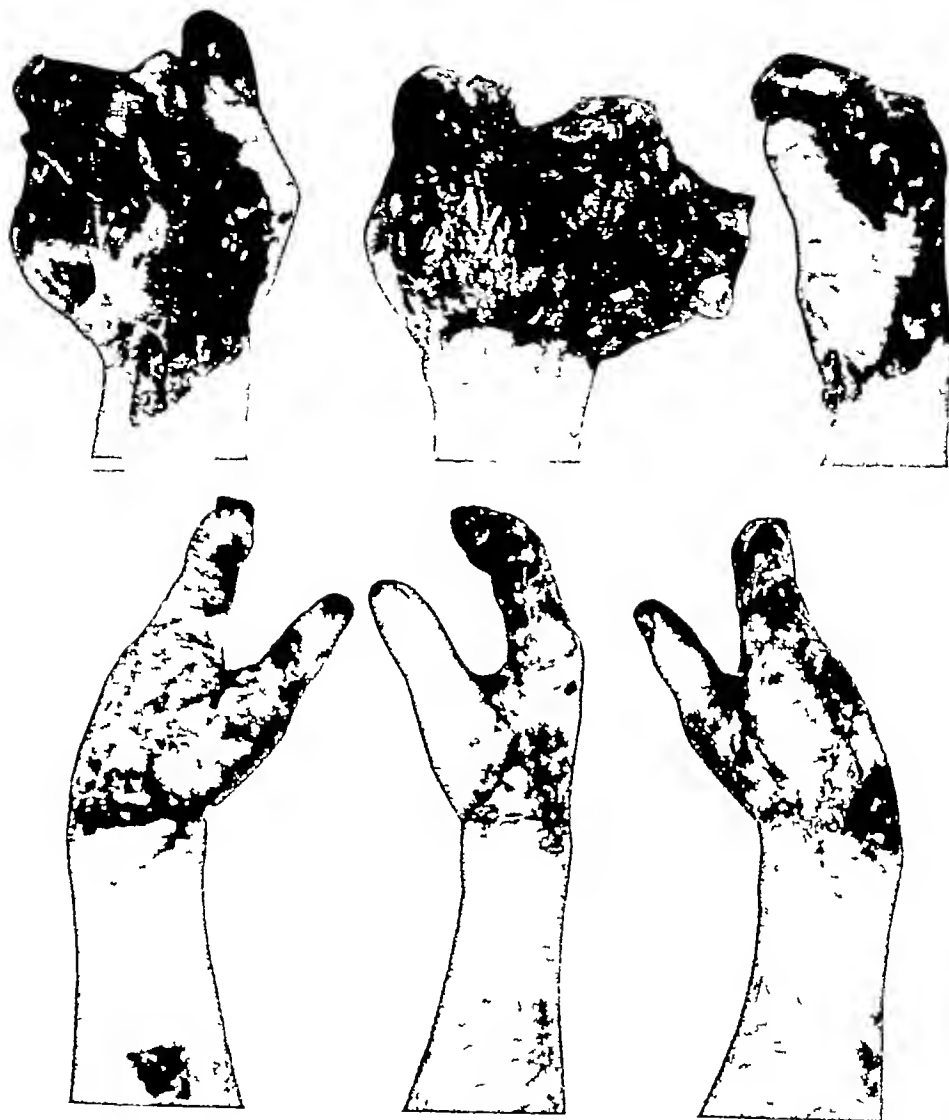


Fig 15

Fig 15 Crushing injury of the hand treated by immediate soap and water cleansing, wound repair and immediate covering of the extensive raw surfaces with grafts of intermediate thickness (Patient of Dr Michael Mason *N. England J. M.*, 1941, 225 108) Above, Appearance of the hand before operation Below, Appearance of the hand at the primary dressing 14 days after operation

Fig 16 Hand shown in Figure 15 as it appeared bandaged with moderate pressure and immobilized on aluminum splint during postoperative period (Patient of Dr Michael Mason *N. England J. M.*, 1941, 225 109)

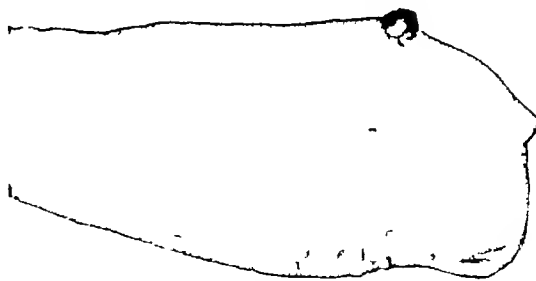


Fig 16



Fig. 7. Crushing injury of dorsum of hand with loss of covering tissue and exposure of extensor tendons. (*Surg. G. Obs.* 94: 7, 66)

within an 8 hour period after an injury has been sustained we are unwilling except under unusual circumstances to consider the safe period longer than 2 to 3 hours. It is possible that with the aid of the sulfonamides the safe interval will be increased, but there can be no question that with each passing quarter hour the chances of transforming the contaminated wound into a clean wound and securing healing by primary union are definitely diminished.

The character and extent of the wound are important considerations. Clean cut, incised wounds made by glass or sharp metal are of all least likely to be contaminated and may lend themselves to repair and closure quite as well as the purposeful incision made by the surgeon. At the other end of the scale are the extensive crushing injuries with loss of covering tissue and ragged lacerations of fascia, muscles, tendons, and nerves and often with multiple comminuted fractures of bone. To draw hard and fast lines is impossible. Patience, gentleness, and care combined with good surgical judgment can often accomplish some degree of restoration in limbs that seem irretrievably lost (Figs. 15, 16, 19, 20).

Little need be added concerning the importance of the patient's general condition, and of favorable conditions for carrying out difficult surgical procedures. It can be summed up in the simple statement that there is no substitute for good surgical judgment. If the patient fails to survive, the surgeon's best efforts go for naught. If the surgeon does not have adequate assistance and proper equipment the care of even simple injuries becomes exceedingly difficult and the results of treatment are correspondingly unsatisfactory.

It should always be remembered that if repair is attempted and infection supervenes little is ever gained, and the result may be disastrous. On the other hand if one makes

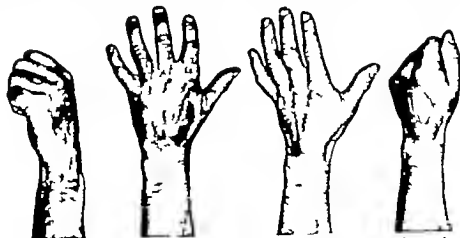


Fig. 8. Result of immediate application of graft of hole thickness skin 1. All defects resulting from crushing injury of hand shown in Figure 7. (*Surg. G. Obs.* 94: 7, 67)



Fig 19 Crushing injury of the hand with destruction of covering tissues, tendons, and part of metacarpal bones, treated by immediate soap and water cleansing and early application of pedunculated flap from thigh Left, appear-



ance of the hand immediately after injury was sustained Right, appearance of the hand underneath flap (Patient of Dr Michael Mason *J Am M Ass*, 1936, 107 1047)

every effort to convert the contaminated wound into a clean wound and stops there, healing may follow promptly, and repair under the most favorable conditions becomes possible within 3 or 4 weeks' time

Specific mention must be made of injuries with loss of covering tissue, injuries of blood vessels, injuries of bones and joints, injuries of nerves and tendons

*Loss of covering tissues* With avulsion injuries and loss of covering tissues the hours immediately following injury are of vital importance, for unless one seizes the opportunity to convert the contaminated wound into a clean one and close it within a few hours of the time of injury the possibility of securing the most favorable result is irretrievably lost A razor graft of intermediate thickness (Figs 12, 13, 15, 16), a graft of whole thickness skin (Figs 17, 18), a sliding flap or a flap from a distance (Figs 19, 20) may meet the indication in any particular case, the important consideration is that such a procedure, if carefully carried out has every chance of success during the early hours following injury, but if infection develops over an extensive raw surface an almost inevitable occurrence if the wound is treated expectantly, the chance of securing a satisfactory result is greatly di-

minished and the opportunity to accomplish it long deferred

The technique of applying grafts and pedunculated flaps over raw surfaces is not diffi-

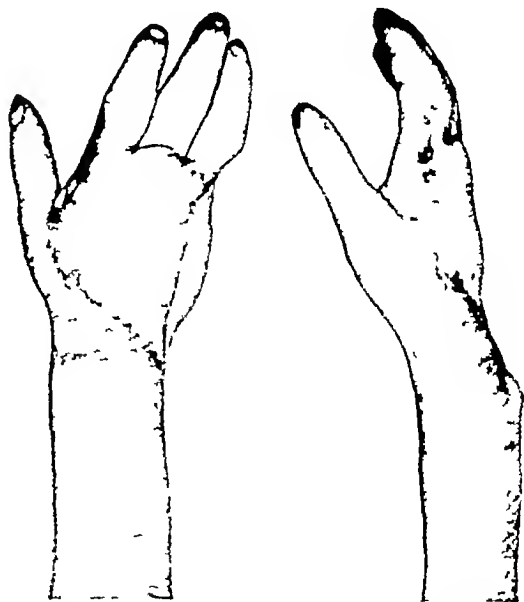


Fig 20 Appearance of hand shown in Figure 19 eleven weeks after injury (Patient of Dr Michael Mason *J Am M Ass*, 1936, 107 1047)

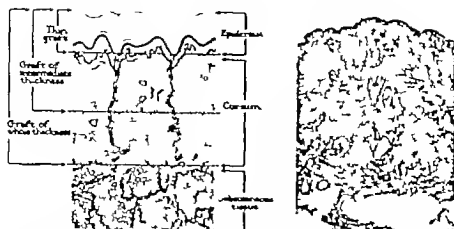


Fig. 21. Diagram showing skin in cross section, and thickness of skin included in different types of graft. I the photomicrograph of similar section of skin, to the right, can be seen the numerous epithelial elements within the corium—hair follicle, sebaceous and sweat glands, from which the epidermis is rapidly re-formed, even though the entire epidermis and part of the corium has been removed for use as graft. (*Surg Gyn Obst* 94 72 58.)

cult to understand or learn. Success depends on attention to a number of details which have been stressed in the many excellent contributions of Blair Brown and Byars, J.S. Davis, and others, and well described by Webster and by Blair and Brown in *Christopher's Textbook of Surgery*.

Essential principles to keep in mind are the indications for the use of different types of grafts, the importance of covering the raw surface completely, of maintaining pressure over the graft or flap to prevent oozing underneath it and congestion within it and the necessity for maintaining the part at rest until healing is complete.

Concerning the indications for the three types of transplants commonly used (Fig. 21) namely grafts of intermediate thickness, grafts of whole thickness skin and pedunculated flaps, one should remember

1. It is wise to use the simplest procedure that will give the desired result.

2. If one can secure prompt and primary healing of a large open wound a covering which may not be ideal from the standpoint of appearance and function can be replaced at a later date and with the maximum chance of securing a good result. If large wounds are left open to become secondarily infected and if deep and widespread fibrous tissue formation takes place it may be quite impossible

ever to accomplish a satisfactory result, even with skillful care and multiple operations.

3. If the raw surface has a fairly normal blood supply and if structures which require a covering of subcutaneous tissue, such as tendons, nerves, large blood vessels, bones and joints, are not exposed in the open wound the graft of intermediate thickness is the one of choice. It can be quickly obtained with a razor or large microtome like knife. It can be held in place with a minimum of sutures, and the raw surface left by its removal heals in 12 or 14 days if only it is covered with a nonadherent dressing, a mass of sterile gauze bandaged snugly and left undisturbed during the period of healing.

4. If structures which require a covering of subcutaneous tissues as well as skin are widely exposed so that they cannot be covered by drawing over them subcutaneous tissue from either side, one must provide a pedunculated flap from the adjacent tissues or from a distance. We know of no way of transplanting a graft of skin and subcutaneous tissue even a graft of intermediate thickness cannot lie if laid over avascular structures such as tendons, nerves, arteries, and bone. That it would not be satisfactory from the standpoint of function is obvious.

5. The most frequent indication for the use of the whole thickness graft is in the repair

of freshly made raw surfaces which are surgically clean, such as result for example from excision of healed burn scars, of surfaces where a covering with minimum tendency to contract is essential (flexor surfaces), and of surfaces where a maximum thickness of skin is needed to give protection and adequate function

With favorable conditions, namely, an open wound with base of fairly normal subcutaneous tissue, a patient seen shortly after injury was sustained, and with adequate time and facilities for carrying out an exacting surgical procedure and where whole thickness skin is needed for good function and normal appearance the use of a whole thickness graft is indicated in the treatment of a recent open wound. With less favorable conditions one would use a graft of intermediate thickness.

*Closure of the open wound and healing in the minimum period of time are the objectives to keep in mind*

*Injuries of the blood vessels* The control of bleeding and the treatment of shock do not come in the province of this discussion but it may not be amiss to repeat the importance of carefully applied compression over a bleeding wound, and the fact, sometimes forgotten, that pressure held directly over the site of bleeding can effectively control severe hemorrhage whereas a large mass of gauze, even if held by a very tight bandage, may fail completely to arrest the bleeding.

Of all peripheral injuries none can so quickly and certainly test the skill and equanimity of the surgeon as injuries involving the blood vessels. To grasp in artery forceps a seemingly inoffensive and fairly superficial foreign body and to have its removal followed by a gush of blood that completely deluges the operative field is an experience not easily forgotten. Only one such accident is enough to make the surgeon view every foreign body in neck or extremity with grave suspicion, to check carefully for signs of vascular injury and *in case of doubt to expose the involved area by an adequate incision above and below the foreign body before attempting its removal*. Care to secure adequate exposure is essential in every type of operation, but nowhere is it more important than in wounds of blood vessels.

Little can be said in a limited space about the difficulties that confront the surgeon in operating on a tense swollen leg, or shoulder or buttock, in which x-ray examination shows a deeply embedded foreign body and in which the tension, the bluish discoloration and the constant trickle of blood from a small wound of entry indicate the presence of vascular injury. The blood pressure cuff as a tourniquet, if a tourniquet can be applied, has the advantages of known compression, of causing minimum trauma to the tissues it surrounds, and of ease of application and reapplication. If after release of the constriction furious bleeding again takes place the cuff can be quickly reinflated and constriction re-established with minimum difficulty. An adequate incision above and below the wound is essential. Good lighting, steady retraction, and an alert and skilled nurse assistant are invaluable aids.

When areolar tissue, intermuscular spaces, even muscles themselves are tense and discolored with dark extravasated blood and when after wide incision all the soft tissues seem to bulge outward as a dark red boggy mass a steady hand and accurate anatomical knowledge are of paramount importance. Without them the surgeon is lost.

*Injuries of bones and joints* In spite of a tendency to consider the treatment of fractures as belonging in a domain of its own or as the province of the orthopedic surgeon rather than the general surgeon, the presence of a fractured bone in an open wound is like the riddle "What animal has feathers, two legs, and barks like a dog?" The animal is the same old rooster, the bark simply makes the riddle harder. In the presence of a compound fracture or joint injury the same principles of treatment apply as in other open wounds, though the successful application of those principles is admittedly more difficult.

Thoughtful surgeons are agreed upon the importance of early reduction of fractured bones and prompt closure of joint wounds. In the presence of compound fractures the principles of first aid treatment mentioned above are vitally important. The immediate application of a sterile dressing *without probing or manipulation* can prevent serious contam-

ination of soft tissues. In first aid treatment protruding bone fragments should be left untouched to manipulate them into proper position may result in carrying surface contamination deeply into an extremity. If the patient is to be transported for any distance however one must run the risk of carrying infection into the wound from without as traction is applied to the limb to escape the greater risk of injury from movement of fractured fragments.

With an injury severe enough to produce a fracture the extent of soft tissue injury is unpredictable from the appearance and extent of the external wound. The presence of nerve injury can and should be known before treatment is begun. Many a surgeon has first noted to his dismay after reduction or operation upon a fractured humerus the signs of radial or ulnar nerve injury and has been plagued with uncertainty both as to the extent and mechanism of nerve injury. Signs of injury of muscles and tendons are difficult to elicit in the presence of a fracture often it may not be wise to attempt it.

In recognizing the presence and extent of nerve, muscle, and tendon injury and that of vascular and bone injury at the time of operation a bloodless field is an invaluable aid. It helps to simplify the work of the surgeon it enables him to make exact and accurate observations and to carry out definitive procedures. It conserves precious blood and makes it possible to avoid the trauma of repeated sponging. Without a field unobscured by constant bleeding accurate reduction of a comminuted fracture and accurate repair of divided tendons and nerves are difficult at best in some cases it may be quite impossible. The first step therefore in treatment is the application of a constrictor preferably a pneumatic band such as a blood pressure cuff. The position and extent of the wound may preclude its use but the advantages of a bloodless field are so great that it should be secured if possible.

Cleansing of the wound is carried out in the manner described. Particular care is taken to cleanse bone fragments which protrude through the open wound before they are reduced. If necessary badly soiled bone ends

can be snipped away with bone biting forceps, but we have seen a complete compound dislocation at the astragalocalcaneal joint heal without inflammatory reaction although the inferior surface of the astragalus had been ground into a bed of fine black dust and cinders and after prolonged cleansing the articular surface of the bone was still partially blackened by minute fragments embedded in the exposed cartilage.

When cleansing of the surface and of the exposed wound is complete sterile linen is applied and the operative procedure indicated carried out (Fig 22). If the external wound is small, as so frequently happens in the compound fractures of civil life it is enlarged by vertical incision above and below the site of injury. The entire depth of the wound so exposed is thoroughly irrigated with warm salt solution until clots and debris are completely removed. If indicated, gloves can be changed and fresh linen applied at this stage so as to assure the greatest possible degree of cleanliness. Loose, torn and fragmented muscle is cleanly excised. Only completely loose bone fragments are removed those attached to periosteum and muscle are brought into position as accurately as possible and maintained by appropriate methods. Needless to say if it is possible to maintain reduction of fractured fragments by traction by the Thomas splint or one of its modifications, or by a simple plaster splint both patient and surgeon are fortunate. Whether the surgeon should use some form of internal fixation in the presence of a comminuted or spiral or oblique fracture depends primarily upon his ability to transform the wound into a clean wound. Just as in cases of nerve and tendon injury in which the use of foreign bodies is essential to secure accurate reduction of the fracture if internal fixation is employed to secure the fractured bone primary healing without infection is essential for a good result.

Many bitter arguments have developed over the question of using nails, plates screws bands and wires to maintain accurate reduction of a compound fracture and many and varying materials have been employed from which to construct the retaining device. Much interesting experimental work has been car-

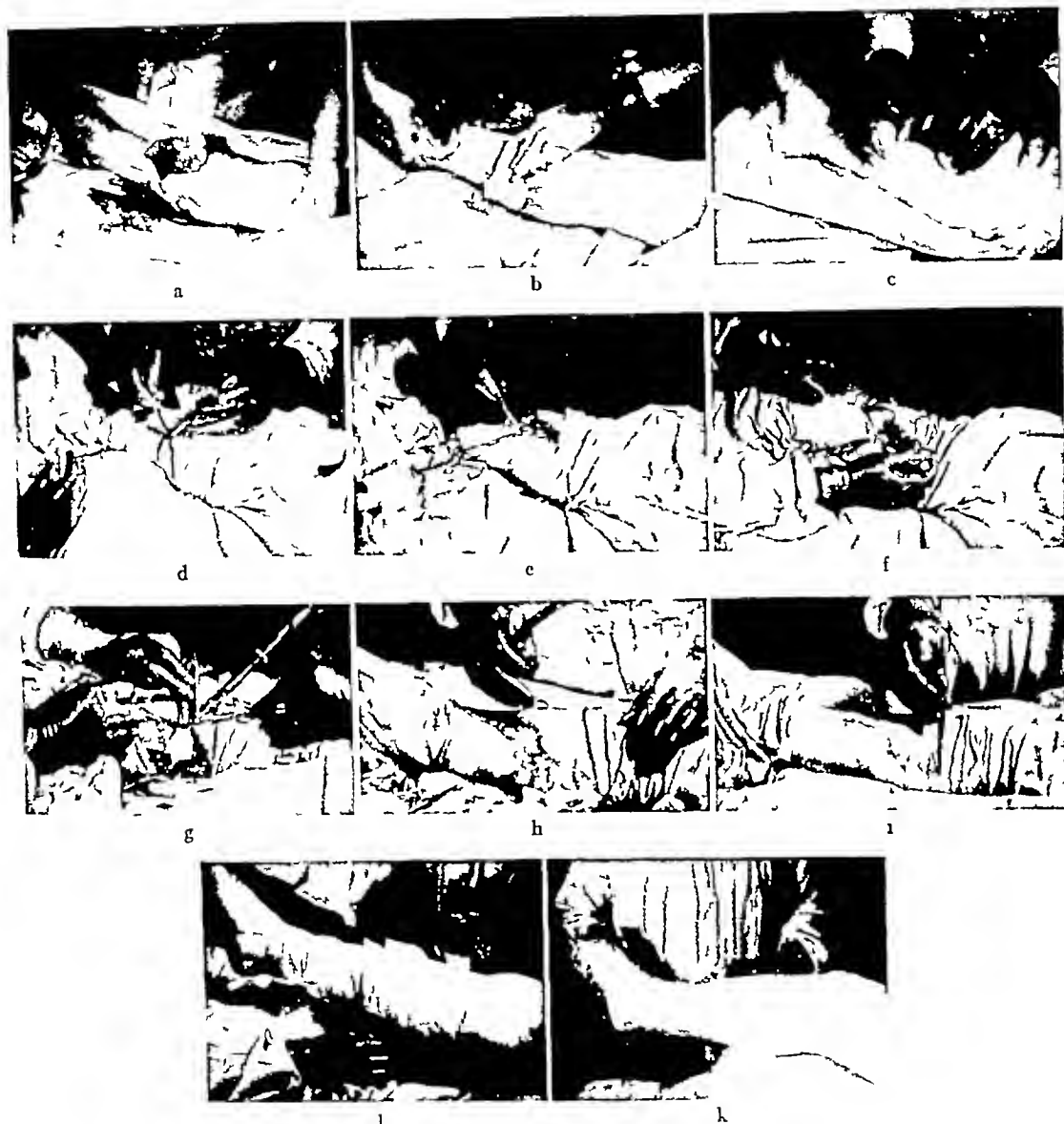


Fig 22 Treatment of a compound fracture of leg (Courtesy of Dr Robert McIlvenny) a, Sterile linen placed under injured leg b, Preparation of field of operation while open wound is protected c, Preparation of skin around wound d, e, Exposure of site of injury with excision of

narrow margin of skin about wound f, Exposure of fractured bone g, Reduction of fracture maintained with aid of screw h, Irrigation of wound with salt solution i, Wound closure j, Application of sterile dressing and compression bandage k, Immobilization in plaster cast

ned out in a search for metallic substances free from irritating effect and which do not retard growth and healing of bone. In spite of arguments pro and con it is probably fair to say that the exact type of metal used or retaining device employed is of secondary import-

ance<sup>1</sup>, and if internal fixation is employed freedom from infection and healing by pri-

<sup>1</sup>The interesting experimental investigations of Bothe, Davenport and Beaton on the effect of tantalum on healing bone indicate that in experimental animals this metal is so completely free from irritating properties that periosteum grows over it and callus and periosteum can ensheath it as though the tantalum plate were a graft of autogenous bone.



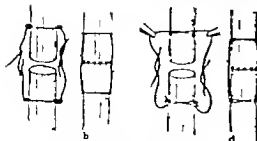


Fig. 3. Technique of tendon suture (Mason). Both methods (a, b, and c, d) are consistent with the important principle that the free ends of the two segments should be as free as possible from foreign material. Experimental studies indicate that in the second method (c, d) there is less tendency for the tension suture to cut through the tendon and permit partial separation of the sutured ends. (*Q. Bull. Northwest L. & M. School*, 940, 40-6.)

many union are the essential factors in securing consistently successful results.

An alternative method of securing and maintaining reduction of bone fragments in a compound fracture is with the aid of pins in the ends of the fractured bone and a distraction apparatus after reduction has been obtained pins and extremity are incorporated in a plaster cast. Orr Anderson and others who have advocated such a plan of treatment would take issue with the statement that this method represents an alternative method. They regard it as the treatment of choice not only of compound fractures but of many not compounded. Without attempting to argue the question we would point out that in order to secure reduction and immobilization of a comminuted or oblique fracture with the aid of pins and distraction apparatus one must have both considerable equipment and adequate training in its use. The surgeon who is accustomed, for example to the use of plaster or traction secured with adhesive and combined with the use of the Thomas splint may easily get into difficulties in attempting to employ a method with which he has had no experience no matter how satisfactory the results of the method in skilled hands.



Fig. 2. Simple splint for preventing contact over stretchers of paralyzed lumbosacral and intercostal by preventing hyperextension of the metacarpophalangeal joints. A splint to prevent such overstretching should be worn for from 1 to 6 months after nature of median and ulnar nerves. (*Q. Bull. Northwest L. & M. School*, 940, 40-7.)

A second consideration is the effect of the pins upon muscles and tendons through or beside which they are passed. No one who is conscious of the restricting and constricting effect of scar tissue upon structures whose function depends upon freedom of movement can look with complete equanimity upon illustrations of pins passing through masses of muscle or through a group of tendons so important for function as the flexor tendons of the fingers.

The ability of serous lined cavities to resist infection is well recognized. Joint cavities carefully cleansed and closed against access of infection from without usually heal kindly. Joint cavities left exposed to the outside

Recently a young man with multiple injuries including fracture of the middle of the femur. A pin for traction had been inserted just above the condyles, but too far anteriorly so that the entire upper end of the lower fragment, so drawn into position, came to the upper fracture. The lower fragment is in a shelling metal trough which extended only to the line of fracture and did not provide firm partial immobilization of the upper fragment. The surgeon objected to its removal with the apparatus in question, but had been recommended as the ideal method of treatment.

world inevitably become infected, and infection usually results in ankylosis and not infrequently in ascending infection along fascial planes and vascular channels. No one who has had experience in the treatment of extensive compound injuries would argue against the statement that care in securing complete cleanliness of the joint cavity, painstaking irrigation with salt solution, and meticulous closure of the joint capsule result in saving of joints that inevitably become infected if treated by expectant methods.

**Nerve and tendon injuries** To secure good results in the repair of divided nerves and tendons it is equally essential that the wound should heal by primary union, that the operation be carried out with exacting care and that postoperative relaxation of the injured structures should be complete and maintained for from 3 to 4 weeks. It is often forgotten that not only must the patient be assured of freedom from the diffuse fibrous tissue formation that follows hemorrhage and infection, but that tendon repair must be so carefully accomplished that the possibility of gliding movement is not lost as a result of fibrous tissue formation about the site of suture, and that in the suture of divided nerves no suture material must be permitted to enter the nerve substance and lead to the scar tissue formation that blocks the downgrowth of nerve axons and makes nerve regeneration impossible.

If both nerves and tendons are injured tendons should be repaired first because they usually lie more deeply and because there should be a minimum of manipulation and disturbance of the tissues after the more fragile and delicate structures, the nerves, are repaired.

As in the treatment of bone injuries a bloodless field must be secured if possible. Tendons should be sutured end-to-end and with the finest caliber of silk which has the required tensile strength. We prefer to use untreated silk and to avoid covering it with wax or any oily material which might lessen the holding power of the knots (Shambaugh). Different methods of suture have been recommended by men particularly interested in the repair and healing of tendons. The principles that should be kept in mind are

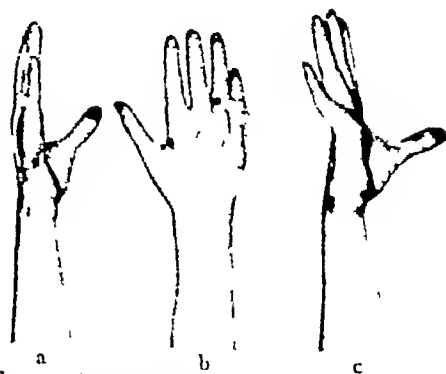


Fig. 25. A splint to prevent overstretching of interossei and medial lumbricals in a patient with ulnar nerve injury. a, b. Fingers supported in slight flexion at metacarpophalangeal joints. c. When the patient extends the unsupported fingers they pass into hyperextension at the metacarpophalangeal joints and undue tension is exerted upon the muscles supplied by the ulnar nerve. (*Q. Bull. North West Univ. Med. School* 1940 40 7.)

1. Gentle handling of tendons and avoidance of trauma are as important as in the repair of the intestine if the delicate sheath of synovial tissue which covers the tendon is to be preserved and make possible gliding movement when healing is complete.

2. To ensure prompt and sound healing there should be a minimum of foreign material (suture material) where tendon ends are brought together, so that no mechanical barrier can obstruct the growth of tendon fibers across the gap between the cut ends or divert them from a direct path from one cut surface to the other. Sutures emerging from cut surfaces, and knots lying between tendon ends constitute such barriers. A method of suture such as that suggested by Mason (Fig. 23) fulfills the requirements mentioned, for the retention suture is placed in such a manner as to leave the tendon ends free and the circular apposition of cut surfaces, which ensures accurate most superficial layer of tendon fibers.

3. The line of suture should be protected if possible with areolar tissue or subcutaneous sutures. The more closely one can imitate the conditions normally present the more certain he will be of a successful outcome.

4. If, as a result of injury or destruction of the fibrous tendon sheaths, tendons are drawn away from the surface over which they pass

as tension is put upon them retaining ligaments must be provided to form a substitute for the injured sheaths. At times the edges of the fibrous sheath can be drawn together to hold the tendon in place or sheath tissue still attached at one side can be drawn across the tendon and held in place by suturing its free edge. In some cases it may be necessary to provide tissue from another part of the body such as smooth fascia or tendons that can be spared without loss of function to lay across the anterior aspect of the ankle the dorsum of the wrist or to surround a digit. In any event the new ligament must present a smooth synovial like surface where it crosses the tendon. It must not constrict the tendon and it should be placed far enough from the line of suture so that the resultant callus (for tendons heal much as do bones, and with spindle shaped thickening at the line of union) does not impinge upon the retaining ligament as the tendon moves back and forth.

5 Finally "injured tissues need rest and the treatment of fractured tendons is essentially identical with that of fractured bones. *Reduction* is obtained with the aid of sutures, *immobilization* with the aid of a splint, and *immobilization* must be maintained in such a position that there is a minimum of pull on the fractured fragments. In other words the insertion of the tendon is brought well toward the origin of its muscle and supported in such a position until healing takes place.

As Mason and Allen have demonstrated softening of the tendon ends takes place in the days immediately following tendon suture. If movement is carried out at this stage the sutures give way from tension or cut through the softened tendon ends. At the end of 8 or 10 days as the line of union becomes more resistant movement results only in irritation inflammatory thickening and formation of adhesions. Only after the fourteenth day can gentle movement be safely begun and then it should be only slight active movement carried out under supervision, and still without permitting more than slight relaxation. At the end of 3 or 3 1/2 weeks splinting can usually be discontinued and active movement carried out but with care not to put undue tension on the newly healed tendon.

Suture of divided nerves should be carried out as the final step before the wound is closed. Essential for success are accurate apposition of clean cut nerve ends with fine sutures that do not enter the nerve substance, freedom from tension on the line of suture, complete hemostasis, protection of the sutured nerve from fixation to surrounding structures and particularly to sutured tendons, rest of the affected limb in such a position that there is a minimum of tension on the suture line until sound healing has taken place and *relaxation of paralyzed muscles until regenerated nerve fibers can reinnervate them* (Figs. 24-25).

Many methods have been suggested for bridging a gap between separated nerve ends but most surgeons agree that only end-to-end suture of divided nerves can give a satisfactory result.<sup>1</sup> With loss of nerve substance that makes difficult apposition of nerve ends without tension the surgeon has three arrows for his bow: freeing the nerve from areolar tissue or neighboring blood vessels above and below the site of injury bringing the limb into flexion so that the nerve passes across an arc instead of along an extended flat surface transferring the nerve to a new position so that it traverses a shorter course. Transfer of the ulnar nerve from behind the medial condyle to the volar surface of the elbow is a familiar example of the last maneuver.

Clean cut nerve ends should be brought together without tension, and held with fine silk sutures that catch only the epineurium. Eight-o silk, swaged on a fine round needle such as the ophthalmologists use for cataract operations, is an excellent material for suture. If three or four sutures are inserted before any are tied their insertion is made easier and there will be less likelihood of the first sutures cutting through the fragile epineurium as the nerve ends are drawn together. The sutures so placed are then used to rotate the nerve first clockwise and then counterclockwise until sufficient sutures have been inserted to give as smooth and complete apposition as possible.

The line of suture and the adjacent portions of the nerve are protected as well as possible

<sup>1</sup> Favorable results with nerve grafts have been reported by Bennett and a few others. The operation is difficult from technical standpoint, no limitations are not yet clearly defined, nor have the best methods of procedure been determined.

with areolar tissue from the neighborhood, with fat from the subcutaneous tissue of the open wound or subcutaneous fat from another part

The importance of keeping the part at rest and the limb in such a position that there is a minimum of tension on sutured nerve ends until sound healing takes place is well recognized. Firm union requires from 3 to 4 weeks and no active movement that might cause tension should be permitted during this period. Equally important considerations, namely that after motor nerve injury *paralyzed muscles must be supported in a position of relaxation until regenerating nerve fibers can again make their way into them* and that their nutrition must be maintained by simple physical therapy, are too often forgotten. As a result paralyzed muscles are constantly over-stretched by healthy and sometimes powerful antagonists and return of muscle tone and contractile power in the wasted and over-stretched muscle fibers becomes impossible.

#### 7 REST OF INJURED TISSUES

The oft repeated aphorism of Hugh Owen Thomas, "Injured and inflamed tissues need rest," is just as true today as it was 90 years ago. Every surgeon agrees that injured bones need rest. It is often forgotten that the same factors that favor healing of fractured bones work in an identical fashion to bring about healing of fractured soft tissues.

Every medical student knows that to secure healing of a fractured bone he must reduce the fractured fragments, immobilize the affected extremity and maintain immobilization in such a position that there is a minimum tension upon the fractured fragments. Experienced surgeons sometimes forget that the same principles of treatment must be carried out if one is to secure prompt healing of fractured tendons, nerves, and soft tissues.

A second factor in aiding healing, one that has been discovered and forgotten again and again, is that of moderate compression, uniformly applied over the wound area.<sup>1</sup> The helpful

effect of compression is no better exemplified than in the experiences of Orr and Trueta with the use of casts completely enclosing fractured limbs and left undisturbed for long periods of time. Their emphasis upon the harm that results from cutting windows in casts is well known. Thoughtful surgeons have emphasized the fact that the essential factors in the success of Orr and Trueta's method are in continued and uninterrupted rest, the helpful effect of moderate pressure over the injured tissues and freedom from exposure of the wound to repeated bacterial contamination (Wilson).

Uniform pressure over injured tissues has at least two important advantages: it checks and limits persistent oozing of blood and serum into the soft tissues, just as sponge pressure over an oozing surface stops bleeding; secondly, it provides a substitute for the injured outer covering of fascia and covering tissue, whose integrity is so important a factor in maintaining the normal circulation in the soft tissues. Needless to say, the compression must provide moderate tension, it must be uniform, it must not cause constriction.

#### 8 CLEANLY SURGICAL CARE

This principle, so obvious in its importance, is often forgotten—because of lack of time, because of shortage of personnel, many times because the care of wounds is entrusted to individuals not trained to accept such responsibility. One fundamental reason for the lack of trained personnel lies in our methods of training of medical students. Too often the senior medical student is overwhelmed with lectures and clinics devoted to complicated, perhaps unusual conditions, and he completes his course without knowing how to apply a dressing over an open wound without adding further infection to the wound and without contaminating himself and many of the ma-

spaces inevitably become filled with serous fluid which is an extremely good culture medium for certain pathogens, the commonest being staphylococci.

Until recently we had no means of changing that congenial medium in the dead spaces into an uncongenial medium.

Colebrook's suggestion is that the sulfonamides provide the means. It is our belief that the use of pressure to prevent the extravasation and accumulation of serum in the intercellular spaces is of primary importance in aiding recovery. That pressure can also aid in hastening the return of extravasated serum and plasma into the circulation is indicated by Fatey and Robertson's experiences with the use of positive pressure with a pavaex apparatus in the treatment of crushing injuries of the limbs.

<sup>1</sup>In this connection the following quotation from a recent paper by Colebrook is of great interest: "there is one aspect of wound pathology upon which great stress was laid by Almoth Wright and Fleming during the last war, namely that every wound produced by violent injury is really a honeycomb of dead spaces—spaces between muscle bundles in the subcutaneous tissues, fascial planes etc.—and these

ternals with which he is working. He remembers bacteriology as a subject which robbed him of time and energy during his second year but not as an integral part of surgery.

When a ward of surgical patients is entrusted to such an individual<sup>1</sup> it is hardly surprising that once the green discoloration of pyocyanus infection appears on one dressing very little time elapses before the dressings of every patient with an open wound are stained with the same bluish green color. If the bacteria whose presence is so obvious are quickly carried from one patient to another it is only logical to conclude that the much less obvious but much more dangerous organisms are transmitted in the same fashion and with disastrous results. The patient who is slowly and painfully building up immunity to the organisms he has been harboring for days or weeks may be quite overwhelmed by the new and symbiotic action of fresh invaders to which he can offer little resistance.

What are the essential factors in cleanly surgical care? Tightly closed lips—still better a masked mouth and nose, clean hands, clean instruments, "forks, not fingers."

To care for a number of patients quickly and efficiently a well equipped dressing cart is essential. A swinging tray can be quickly cov-

ered with a sterile towel on it are laid the sterile instruments and dressings needed for the patient in question. The bandage is cut, the dressing lifted off en masse, wrapped in newspaper and placed immediately in a closed metal container attached to the cart. The wound is cleansed, if necessary with sponges moistened with soap solution and dried with sterile gauze. Sutures are removed, dressings reapplied.

The whole procedure is carried out with sterile instruments and nothing is touched with hands or fingers until the outer bandage is applied over the sterile dressings.

Needless to say dressings are done when there is as little commotion in the ward as possible. Sweeping, bed making, visitors moving back and forth, all stir up air currents and dust and may cause further contamination of an exposed wound.

De Lee, the distinguished obstetrician, often talked to his students about an "aseptic conscience." It is one of the fundamental elements in cleanly surgical care—the care that provides for the patient in the surgical ward the same meticulous attention to details that is insisted upon in the operating room to safeguard him from the ever constant threat of infection.

ERRATA: NOTE: The second and final chapter of this paper will appear in the next issue of the Journal.

<sup>1</sup>Read, member of a local drift board in surgical accident recently. "Doc, we don't care how well cleaned you are. All we want to know is that you're an M.D."

# THE MYSTERIOUS MIXED TUMORS OF THE SALIVARY GLANDS

JOSEPH McFARLAND, M.D., Sc.D., Philadelphia, Pennsylvania

SOME years ago a group of men congregated in the lobby of this College of Physicians, and chatting upon various topics, began to talk about the various kinds of public speaking in which doctors engage. All had lectured to students, all had made after dinner speeches, one or two had lectured to women's clubs or other social organizations, some had promoted the sale of liberty bonds during the last war. Most unexpectedly one said, "Did any of you ever hear me preach?" whereupon another turned to him and said, "I never heard you speak, when you did not preach."

I shall not only lecture to you tonight, I shall preach to you, and it shall be from a text taken from the moral maxims of Josh Billings, "You'd better not know so much than know so many things that ain't so."

Let us consider the subject, therefore, with reference to the things that we know, but which often, alas, "ain't so."

## WHAT ARE MIXED TUMORS?

It is difficult to know exactly what we are talking about and to be sure that each knows what the other is thinking about when we speak of mixed tumors. Stedman's *Medical Dictionary* defines a mixed tumor as "one composed of two or more kinds of tissue." That is entirely inadequate for every adenoma and every carcinoma is composed of the parenchymal epithelial tissue and the interstitial connective tissue that holds it together, and in addition to these two, there is always the vascular tissue by which it is nourished, and there are a few nerves. Whatever else it may contain, every mixed tumor seems to consist primarily of the parenchymatous and interstitial tissues.

Annual conversational meeting "Lecture" before the Pathological Society of Philadelphia, April 9, 1942.  
Dr. McFarland is Emeritus Professor of Pathology in the Medical Department of the University of Pennsylvania. Professor of General Pathology in the Dental Department of Temple University.

The parenchyma may be so scanty as to be overlooked unless sought for, or it may seem to make up the entire tumor. It may consist of what can be divided into acini and ducts, but never resembles the salivary gland structure so closely as to be mistaken for it, or, as the tumor is always surrounded by a definite capsule, to suggest connection with it. The interstitial element varies from mucilaginous substance so soft as to lead the operating surgeon to suppose that he is removing a cyst instead of a tumor, to dense cartilage-like substance containing indefinitely circumscribed masses of bone. It is the different proportions of the parenchymatous and interstitial tissues and the condition of growth, quiescence or retrogression of each, that determine dissimilarities among the tumors.

There seems to be a world of difference between a tumor so soft and fragile as to be thought a cyst and one so uniformly cartilaginous as to be called chondroma, between one whose atypically arranged epithelial elements present a pattern like carcinoma and one whose almost purely spindle cell structure immediately suggests sarcoma. Yet they are but varieties of the same tumor.

## FROM WHAT DO THE MIXED TUMORS ARISE?

In what do they begin, remembering that we are considering only those of the salivary glands—parotid, submaxillary and sublingual,—and not those of the lacrimals, hard and soft palates, face or extremities? Of 413 tumors in my collection, there were 389 parotid, 12 submaxillary and 12 sublingual. The tumors were first described by Virchow who in 1863 spoke of them as "enchondromas" or "diffuse enchondromas," and conceived them to be of mesenchymatous connective tissue origin. As they always contained some epithelial elements that had to be accounted for,

terials with which he is working. He remembers bacteriology as a subject which robbed him of time and energy during his second year but not as an integral part of surgery.

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\*Child, member of a local draft board to surgical resident recently. "Doc, we don't care how well treated you are. All we want to know that you're an 'M. D.'"

Cuneo and Veau, in 1900, after a careful study of the embryology of the neck and of about 50 cervical tumors, arrived at the conclusion that "the tumors arose through local defective development of the parts in which they occurred, as the result of 'enclavement' or isolation or sequestration and the subsequent vegetation of the embryonal material." Their name for mixed tumors was "enclavoma."

Forgue and Massabuau found that the sequestered embryonal cellular material arose in close relationship to the branchial arches and therefore preferred to describe the tumors as "branchiomas."

Chevassu, more conservative in his views, conceived that mixed tumors might arise in at least 4 different ways (1) From the tissue of a salivary gland, (2) from its embryonal glandular rudiments by "enclavement," (3) from the branchial arches (Virchow had tried to derive the cartilage in the tumors from Meckel's and Reichert's cartilage), and (4) from "embryoma juxtasalivare" as suggested by Forgue and Massabuau.

The results of all of these theories is a nomenclature that is more mixed and more confusing than the tumors themselves. Tumors are indexed and classified by different pathologists as mixed tumors, chondromas, sarcomas, myxomas, enclavomas, branchiomas, adenomas, adenocarcinomas, carcinomas, and sarcomas, as they adhere to some one theory of origin. Or, abandoning all these classifications, the pathologist may name the tumor in correspondence with its histological structure and apparent clinical potentialities.

#### WHAT IS THE FREQUENCY OF THE MIXED TUMOR?

If you think, as I so often hear it said, that mixed tumors are "common," you think something else that "ain't so." In the course of some 25 years, during which time I have let it be known among my friends that I desire to study as many cases as possible I have been able to find about 400 so called mixed tumors. I say "about 400" because the number varies from day to day as new additions come in and as cases thoroughly studied may be found to belong in some other category.

I have already explained in previous publications that my chief method of finding cases is to visit the laboratories of one hospital after another, ask permission to examine such microscopic slides of salivary gland tumors as may have accumulated, select the ones that conform to the taxonomic requirements, and then review the protocols of the cases for the essential clinical information. An arrangement is then made by which the cases are carefully followed up by the hospital office or through personal correspondence. My collection contains cases with whose microscopy I am familiar from personal observation, but it also contains a few cases very well known clinically, of which no sections are now available.

It is unusual for a protocol upon a mixed tumor to give complete details. On this account, in tabulating the tumors, the numbers appearing in one table never correspond with those in some other table. For example, if one desires to know the relative frequency of tumors on the right side or left side, out of 400 protocols perhaps only 300 make any mention of that point, if one desires to know whether the patient was white or black, no mention is made of the color in 250 cases, and so on. Sometimes the protocols, otherwise sufficiently full in detail, differ in such manner as to make case comparisons difficult. For example, when 2 repeatedly recurrent cases are to be compared, 1 protocol carefully mentions the exact time at which each recurrence was discovered, but the other protocol only records the dates of the operations for tumor removal.

My cases are all "original cases" in that no one else has ever published them, most of them remain "original cases" for anyone who wants to publish them, for with the exception of a very few cases, some of the details of which it was necessary to give, the uses I have made of them are only collective and analytic.

About 385 of my patients came to operation in various hospitals in and about Philadelphia. The remainder came from sources outside of Philadelphia, the microscopic slides and clinical data being sent to me by kind friends.



he described them as "zusammengesetzte Geschwülste" which was translated "mixed tumors."

In 1879 Wartmann conceived that the polyhedral and epithelium-like cells were really of endothelial origin. This idea was immediately adopted by Volkmann whose paper regarding the subject produced such a profound impression that the tumors were for a long time spoken of as endotheliomas. But in 1899 Hinsberg combatted this view and as he was vigorously supported by Bormann the endothelial origin hypothesis lost ground and fell into disrepute until it is seldom mentioned at present.

In 1908 a new idea was propounded by Krompecher who believed that the mixed tumors should be included among those arising from the basal cells of the stratified squamous epithelia, and who renamed them "basaliomas."

But, by whatever theory the parenchyma might be accounted for no solution of the varying interstitial substance was reached. Virchow was greatly perplexed by the frequent presence of the cartilage, which he found to be localized in "islands" in the parotid tumors diffused in the submaxillary tumors, and which he never found in any pancreatic tumors. He suspected that it might be a product of the capsules of the tumors, but could never prove it. Volkmann was not at all troubled by the cartilage which he conceived arose like all of the other elements, "through the unlimited reproductive and metaplastic versatility of the endothelium."

As early as 1878 Marshall, in studying the cranial development of the embryo chick, observed that some of the ectodermal cells of the neural crests of the cephalic region contribute to the formation of mesenchyme, and Clements seized upon the phenomenon to account for the occurrence of the epithelial elements in the mixed tumors.

Ehrlich in 1906 described a mucoid degeneration of the epithelial cells of the salivary gland tumors into a soft jelly-like substance whose subsequent condensation inspissation, and chemical transformation resulted in cartilage. Author after author accepted his view until now it is the most popular one.

With the genesis of the cartilage (it is no longer regarded as cartilage but as a related substance called chondroid) explained, there was no longer any reason to seek for any other origin for the tumor except the salivary gland itself and the recent French writers, Leroux and Leroux Robert heartily support such origin. One cannot let the matter pass, however without reminding himself that the acknowledged exemption of the pancreas from mixed tumors becomes, thereby more difficult to explain. It would seem as though there should be some definite reason for the appearance of mixed tumors in the facial and salivary glands and their absence from the abdominal salivary gland. Can there be a mistake in the supposed anlage or primordium from which they grow?

In 1877 Cohnheim expressed his opinion that the most reasonable explanation of tumor origin was the assumption that in an early stage of embryonic development, more cells are produced than are required for building up the part concerned, so that there remains unappropriated a quantity of cells—they may be very few in number—which, owing to their embryonic character are endowed with a remarkable capacity for proliferation. Let me impress upon you without further tedious quotation, that Cohnheim believed that tumors arose from these "superfluous embryonal cells" and not from the frequently formed tiny supernumerary organs whose formation depends upon the dislocation of some of the substance of the developing organ. The supernumerary organ progresses in development *pari passu* with the main mass as well as it can. I often hear such referred to as

"Cohnheim's embryonal vestiges," which is entirely wrong for they are neither embryonal nor vestiges, and have no more to do with tumors than the organs of which they should have formed a part. The Cohnheimian embryonal material is cellular and usually invisible and he believed that at any time through some kind of stimulation, these potential but latent cells might be induced to grow and a tumor mass, simple or complex atypical because of its unnatural environment might form. This fascinating theory accounts for many tumors better than any other

In all of the hospitals from which our material was gathered, there were only 6 surgeons who were credited with 10 or more cases each, the greatest number being in the experience of the late Dr John B Deaver, who, at the Lankenau and University hospitals, operated upon a total of 29 patients with mixed tumors.

It is to be remembered that these figures do not represent the work of one year, but of the total period included in the research—approximately 25 years! Beware of him whose knowledge is based upon acquaintance with a case—he knows many things that "ain't so!"

difficult to decide whether a given tumor is a mixed tumor or not. In my own collection it was found necessary to eliminate 2 capillary angiomas, 2 Hürthle cell tumors (onchocytomas), 2 neurofibromas (schwannomas), and 2 branchiogenic carcinomas.

The inclusion or exclusion of such tumors must depend, in part, upon the theory of origin to which one inclines. If he follows Cuneo and Veau and Chevassu in believing that the tumors arise through the "enclavement" of embryonal substance in the developing face and neck, they may be retained, if, on the other hand, he accepts the origin of the tumors from neoplasia of the respective salivary glands, they must be eliminated. To make our studies agree with this latter, now popular view, we have eliminated them.

Leroux and Leroux-Robert (14) divided their 102 cases into 17 separate varieties, which would allow an average of only 6 tumors in a class. Of course of the more frequent varieties there were more, and in the rare varieties less, so that sometimes conclusions as to the benignancy or malignancy of a class had to be deduced from what was known about 1 or 2 tumors of a group whose clinical behavior is acknowledged to be highly variable. It is evident that the most erroneous conclusions might be arrived at! They were, however, quite justified in the creation of their categories, and for my own purposes I have found it useful to arrange the tumors in 14 groups.

It would be appropriate to show this histopathological arrangement at this point, but it seems preferable to reserve it for a later heading when its presentation may accomplish several purposes.

#### ARE THE MIXED TUMORS BENIGN OR MALIGNANT?

Josh Billings, if he had ever considered this subject and heard it argued about, would again remind us that those who find the question of benignancy and malignancy easy to define or agree upon, know some things that "ain't so."

Living in considering the question, say, 'The distinction between benign and malignant tumors involves questions of great

#### WHAT IS THE HISTOLOGICAL STRUCTURE OF MIXED TUMORS?

That the histological structure is extremely variable is shown by the fact that Harvey, Dawson and Innes made use of 54 photomicrographs to present and explain the variety of appearance they observed. They, however, included some lacrimal, palatal, labial, molar, and mammary mixed tumors, not in the scope of the present discussion.

In the paper "Etude analytique des éléments constitutifs des tumeurs dites mixtes des glandes salivaires," Leroux, Leroux-Robert, and Dillange (15) presented 10 beautiful photomicrographs illustrating the different appearances observed in the 40 cases they studied and the following explanation: "The apparent complexity of their structure depends upon local morphological variations among cells of the same type, and not from multiplicity of cell types." In a later paper, "L'essai de classification architecturale des tumeurs des glandes salivaires," Leroux and Leroux Robert (14) used 24 photomicrographs to illustrate the varying appearances observed in 102 cases that were studied from the standpoint of histopathological prognosis. In a paper dealing with the same subject, "The Histopathologic Prognosis of Salivary Gland Mixed Tumors," I (16) used 12 photomicrographs for the same purpose. All this goes to show that the tumors have a most varied and complex histopathological structure, however it may be accounted for. In dealing with such complexity it may become

The cases have come from a total of 29 hospitals. 18 Philadelphia hospitals account for 385. Six Philadelphia hospitals account for 310. The Hahnemann Hospital had 34. Jefferson Hospital 72. Lankenau Hospital 56. Pennsylvania Hospital 34. Philadelphia General Hospital 50. and University Hospital, 64.

If the total number of cases is divided by 6 there is an average of 51+ for each hospital. The remaining 75 cases are to be divided between the remaining 12 Philadelphia hospitals, making an average of 6+ each. Four of these 12 hospitals had only 2 cases each. Many Philadelphia hospitals had not a single case of this kind.

I was much surprised to see how rare these tumors really are and still more so when I found that these cases were all of their kind that had occurred in these hospitals during a period of about 25 years. The number of cases was therefore reduced to 15 a year when divided among all of the hospitals of Philadelphia.

This certainly shows that the tumors are far from common, and my results are fully supported by the experiences of others. Schreiner and Mattick, in analyzing the records of 6,695 patients accepted for treatment at the State Institute for the Study of Malignant Disease at Buffalo, New York, found only 66 cases of tumors of the salivary glands. Ahlborn of the Radiumhemmet in Stockholm, Sweden reported a series of 254 cases. Houch found 48 tumors of the parotid, submaxillary and sublingual glands in the files of the University of Virginia Hospital, of which 6 proved to be other than mixed tumors. Leroux and Leroux Robert (14) collected 102 cases of mixed tumors of the salivary glands and palate from material sent from various sources to the Faculty of Medicine for diagnosis. Dawson and Innes of the Research Laboratory of the Royal College of Physicians, Edinburgh the Cancer Control Organization of Edinburgh and Southeast Scotland and the Institute of Animal Pathology University of Cambridge in their collection of 316 cases, had 253 of the salivary glands. They also mention 5 mixed tumors which occurred in dogs, though in what organs the tumors

occurred is not stated (8 p 277). All this certainly shows that these tumors are not common.

Very little interest seems to have been taken in the patients from whom the tumors were removed. A number of the smaller hospitals have no follow-up service at all, and in a number of the larger ones it is inadequate after the patient reports that he is well for a year or two he is forgotten. It seems extremely rare for the follow-up to be adapted to the particular condition for which it is intended. Mixed tumors may recur after many years so patients from whom they are removed should be followed up for the remainder of their lives. Failure to keep in touch with operation cases leads many surgeons to assume successes to which they are not entitled, and when the known facts seem to favor one as opposed to another the former is apt to assume an attitude of superiority and explain his supposed success as the result of the thoroughness of his method, whereas, were the real facts known there would be no difference in their results.

I have frequently been amused to hear surgeons (friends speak of mixed tumors with the greatest familiarity as though they had operated upon hundreds of them. Indeed, until I came to know the facts, I supposed that to be the case then I was both interested and astonished to find that

At the University Hospital the 57 patients had been operated upon by 9 surgeons, average 6.3 each. At the Jefferson Hospital 67 patients had been operated upon by 23 surgeons average 2.9 each. At the Hahnemann Hospital 32 patients had been operated upon by 16 surgeons average, 2.0 each. At the Lankenau Hospital 43 patients had been operated upon by 10 surgeons average, 4.3 each. At the Oncologic Hospital 8 patients had been operated upon by 2 surgeons average 4.0 each. At the Pennsylvania Hospital 26 patients had been operated upon by 13 surgeons average, 2.0 each. Or if we consider the total 233 patients from all hospitals were operated upon by 73 surgeons, an average of 3.2 cases each. But 37 of the 73 surgeons mentioned had only 1 case each, and 23 more had only 2 cases each.

In all of the hospitals from which our material was gathered, there were only 6 surgeons who were credited with 10 or more cases each, the greatest number being in the experience of the late Dr John B Deaver, who, at the Lankenau and University hospitals, operated upon a total of 29 patients with mixed tumors.

It is to be remembered that these figures do not represent the work of one year, but of the total period included in the research—approximately 25 years! Beware of him whose knowledge is based upon acquaintance with a case—he knows many things that "ain't so"!

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difficult to decide whether a given tumor is a mixed tumor or not. In our own collection it was found necessary to eliminate 2 capillary angiosarcomas, 2 Henle cell tumors (osteocytomas), 2 neurofibromas (sarcomas), and 2 branchiogenic carcinomas.

The inclusion or exclusion of certain tumors must depend in part, upon the theory of origin to which one inclines. If he follows Cuneo and Veas and Cheverton in thinking that the tumors arise from the "development" of embryonal substance in the face and neck, then he will include on the other hand, the tumors from the salivary glands, the thyroid gland, etc. To make our studies agree with the popular view, we have followed Leroux and Leroux.

view, we have seen that the Leroux and Leroux-Paton (14) studies of their 102 cases into 17 categories, which would allow at least 6 tumors in a class. Of course, frequent varieties there are and in the rare varieties less, so that conclusions as to the hereditary character of a class had to be deduced from known about 1 or 2 tumors. The clinical behavior is also highly variable. It is evident that the most erroneous conclusions might be drawn from them, however, quite justifiable. They were, however, quite justifiable. I have found it useful to create 14 groups in 14 groups.

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Josh Billings, if he had considered this subject and heard it argued out, would again remind us that the question of benignancy and mercy is the question of define or agree upon, but it is not so easy to 'ain't so."

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The distinction between benign and malignant tumors involves a question, say, of great

interest both from the theoretical and practical sides. If malignancy were a purely clinical conception it would be impossible to draw any rigid distinction between benign and malignant tumors, since nearly all tumors may occasionally prove fatal. Yet the tendency is to restrict the term to tumors which exhibit certain features which are essentially deleterious to the host. The most important of these features are (1) infiltrative growth (2) local destructive properties, (3) recurrence after removal, (4) formation of metastasis, (5) local interference with function and (6) general toxic action of absorbed tumor products. Taking these up in the order in which they are given, we find

1 *Infiltrative growth* Mixed tumors are usually definitely encapsulated and therefore rarely infiltrative. But if the capsule is opened through traumatic accident or through surgical intervention, as is much more frequently the case, the infiltrative growth may take place as in Case 59. This tumor after 2 operations, 1 for the removal of the primary growth and the other for a recurrence, invaded the orbit causing exophthalmos, eventually penetrated the cranial cavity and caused death by compressing the brain. Such cases are fortunately rare.

2 *Local tissue destruction* The tumors usually project externally so that the skin is the organ most affected. Its great capacity for stretching however usually prevents serious accidents, and tumors of 5, 6 and 7 pounds have been observed without ulceration. The close anatomical relation of the parotid tumors to the 5th and 7th nerves results in pain or palsy in some cases, and it may be for the relief of these evils that the patient seeks advice. If the skin be penetrated because of rapid growth of the tumor or traumatic accident to it, permanent ulceration with fungation, occasional hemorrhage and infection may follow and even be fatal. In the great majority of tumors no such accidents occur and the famous tumor observed by Cotterhill attained an estimated weight of 22 pounds without such mishap.

3 *Recurrence after operative removal* Of the 400 mixed tumors that I have been privileged to study and that form the foundation of my

opinions about 100 are known to have recurred that is 25 per cent. This is the percentage given in text books for recurrence though F. C. Wood found it to be 45 per cent, Benedict and Meigs, 42.5 per cent and Stein and Geschlechter only 20 per cent. This variability may have something to do with the method of classifying the tumors, but perhaps more to do with the method of computing the percentages.

It seems very simple to say 400 cases with 100 recurrences means 25 per cent, but it is very inexact. Of the 400 cases, we have no recent follow-up record on 96 so it is not known whether they are living or dead, with or without recurrences. Eliminating them, the recurrences rise to 32 per cent. In most estimations of success or failure of operative treatment, the surgeon is content if his patient is free of disease after the "5 year period." Suppose that every one of our cases not under observation for 5 years was ruled out, then the recurrences would rise to 40 per cent. But 66 patients from whom mixed tumors have been removed have died without having shown the recurrences from which they might have suffered had they lived longer. If they are deducted so that our calculations are based only upon those patients still living and still under observation, the number of recurrences rises to 50 per cent. But even this figure based on the 5 year period of exemption, is in error because the 5 year period does not apply in the case of mixed tumors as the average time that elapses between the removal of the primary tumor and its post operative recurrence is 7.2 years. If we calculate on that basis, the recurrences rise to 61.72 per cent.

But again, though 7.2 years is the average interval between operation and recurrence it will be seen that one half of the recurrences take place after a longer period, and are sometimes deferred for 20, 30 and in 1 case 45 years. This leaves every case open to the possibility of recurrence and causes one to wonder whether any one who has been the victim of this type of tumor may ever be pronounced cured.

Tumor recurrences may have several causes it may be desirable to mention no more than

The first is a repetition of the same conditions and process by which the primary tumor was brought about, viz, an appropriate primordium acted upon by the appropriate stimulant. From that point of view the primary and recurrent tumors would be independent entities which simply appear in the same region. It would be unnecessary to mention this idea except that it is occasionally offered as an explanation of the long interval that elapses between the operative removal of a mixed tumor and its recurrence.

The more popular and probably more valid explanation is that the recurrence is only the continued growth of tumor tissue left behind at the primary operation. But while that is easy to understand in cases of cancer, in the presence of which it is well recognized that the cells penetrate into the crevices of the tissue and extend, by permeation, widely beyond the confines of the visible and palpable tumor and that the same cells enter into the lymphatics and are carried hither and yon—it is difficult to understand in the case of a circumscribed and encapsulated tumor completely removed, capsule unopened.

Another explanation, however, may suffice to clear up the subject. The tumors appear to be unicentric and probably frequently are, but many are undoubtedly multicentric, and I have sometimes seen a congeries of little tumors the size of peas or even of pinheads, in close juxtaposition to the larger easily recognized tumor. The mixed tumors are also nearly all lobulated, the various lobules are often quite different in structure or development. It is quite conceivable that these lobules began as different centers, some outgrowing others, or having started before others, and in growing larger and larger, came into closer and closer approximation, crowding out the intermediate tissue elements by pressure atrophy until, capsule coming into contact with capsule, the entire aggregation became surrounded by an additional common capsule of the tumor. If the operative removal of the tumor was attempted while any one of the smaller lobules remained separate from the whole, there would be a good chance of its being left behind to appear later as a new and recurrent tumor. Should this suspicion

be true, it ought to be capable of producing some proof, and so I (17) carried out a study on the recurrences of the tumors with special reference to their size at the time of operation. Theoretically, the smaller the tumor at the time of removal, the more likely recurrence would be. Unfortunately the sizes were always expressed in comparison with familiar objects—peas, beans, olives, plums, eggs, apples, oranges, grapefruit, cantaloupes—not in actual measurements. But, regardless of the errors that prevent scientific accuracy, I was able to secure the figures in Table I.

TABLE I

	Cases	Recurrence	Per cent
Group I—tumors smaller than a walnut			
Group II—tumors larger than walnut but smaller than lemon	28	9	32.1
Group III—tumors larger than a lemon	109	19	17.4
As group III is so small and contains only 2 recurrences, combinations were tried for comparison—	19	2	10.0
Groups I and II—all less than size of lemon			
Compare with group III	137	28	20.00
Or	19	2	10.00
Groups II and III—all larger than walnut			
Compare with group I	128	21	16.00
	28	9	32.1

So it seems that however the combination is arranged and compared the smaller tumors suffer the greater number of recurrences. Since these computations were made, another 100 tumors have been added to my collection, and I have hastily reviewed them without any change in the principle or considerable variation in the figures.

The matter must not be closed, however, without calling attention to the danger of leaving part of a tumor behind at the time of operation, either through the accident of tearing the capsule of a very soft tumor or intentionally tearing it because the tumor is in such intimate relation to the facial or other nerves. Such residual tumor tissue usually results in "immediate recurrence" which, of course, is only the continued growth of the primary tumor.

The second factor that may play an important rôle in recurrence is the variety of tumor to be dealt with. One hesitates, how-

TABLE II.—CLASSIFICATION

	Cases	Recurred	Per cent	Total
a. Interstitial tissue tumors				
Simple interstitial tumors				
Interstitial tumors complicated by	97	33	36	
Excessively cellular matrix				
Presence of squamous epithelial cells	9	3	33 3	
Cylindromatous hyaline change	4	5	12 7	
Unusual number of gland-like elements	0	0	0 0	
Scattered oval groups suggesting carcinoma	0	4	44 4	
Appearance suggesting sarcoma	0	3	90	
Presence of osteoid or osseous tissue	3		33 3	
Total	3			
b. Parenchymatous tumors—canalicular or racemose tumors			4	
Simple canalicular	7	0	3 0	
Papillary intracanalicular	6	9	3 8	4
Carcinomatoid canalicular		8	50	
Total			6 +	
c. Carcinomatoid tumors	13	10	76 0	6
d. Sarcomatoid	8		5	
Totals			51	
Grand Totals	305	90	48 8	

ever when the term "variety" is used because, should there be different varieties it should be possible to define them and thus construct a classification. However it will be well to forego any attempt at classification or at scientific denomination and do no more than arrange the tumors with reference to appearances that may have no nosological value because appearances may be the result of temporary conditions of tumor growth rather than permanent qualities.

As has been pointed out, every mixed tumor consists of interstitial and parenchymatous tissues, the proportions and conditions of which vary. With these facts in mind we can arrange our tumors in little groups (Table II) that can be readily compared with one another if we know how many tumors in each group recurred or eventually proved fatal.

Table II shows that the interstitial tumors occur about 3 times as frequently as the parenchymatous tumors, but recur far less frequently 41.2 per cent of the former as compared to 61+ per cent of the latter. With such an analysis before us, it might easily be assumed that the microscopic examination of a section of mixed tumor would enable one to make a reasonably correct prognosis but curiously enough when it was tried in actual practice it did not seem to work out

that way. But who knows how correct or incorrect general deductions made from the study of microscopic sections are? I decided to find out for myself and choosing a slide from my collection at random I noted the supposedly dependable indications of malignancy and wrote down whether I believed the tumor would recur or not. After having done this many times, I compared my opinions with the known facts and was shocked and humiliated to find how frequently my prognosis had been incorrect. A glance at Table II will show the reader that there are recurrent and nonrecurrent tumors in every group except the group of interstitial tumors complicated by the presence of osteoid or osseous tissue. Was my inability to differentiate between the tumors that had recurred and those that had not yet recurred due to my own stupidity or did it lay in the nature of the material?

To answer that question I selected sections of 30 tumors whose behavior was known up to the present time and offered them to 25 competent pathologists, 8 of whom hold professorial positions in the departments of pathology in medical schools and 8 of whom are the heads of the laboratories of large hospitals, while the others represent varying degrees of skill and experience from beginners to those regarded as ready for first class po-

sitions They were asked to answer only one question about each tumor "Do you think it will recur?" It was interesting to observe the attitude of the men toward the problem that they would make no mistakes, others were puzzled and reviewed their work again and again, one gave up about one-third of the slides saying that he was "unable to come to any conclusion about them"

The results were most interesting and astonishing! The average end-result was 52 per cent correct and 48 per cent erroneous. The extremes were not widely separated the lowest percentages of correct opinions were 43 per cent, 45 per cent, and 45 per cent, attained by 2 men of professorial rank and 1 who is the head of a tumor clinic. The highest percentages of correct results were 63 per cent and 63 per cent attained by a professor of pathology and a hospital laboratory director

One naturally inquires whether all made the same mistakes and is surprised to learn that they rarely agreed or disagreed with any uniformity. This is best shown by the results of 2 mentioned as having attained the highest marks. They fully agreed about a number of cases, concerning one-half of which they were wrong. All this is most disheartening! It does not seem possible to foretell what a mixed tumor of the salivary glands will do by examining a section of it with the microscope. Not only is that true, but accurate prognosis seems to be impossible in any case.

This brings us again to the subject of malignant tumor and curability, this time with special reference to metastasis.

**4 Metastasis** Dogmatic statements concerning mixed tumors should be avoided, but may be stated with very little reservation that metastasis is so rare that its occurrence almost be denied. Of the 100 cases under consideration at present metastasis may have occurred in only 2. It is not certain that these cases may not have been metastases but they looked like metastases. These cases may be regarded as metastases in general, however, for in practically all tumors, metastasis not only stamps the

tumor as malignant, but also marks the approach of the fatal termination. On that account surgeons now usually refuse to operate upon patients in whom metastasis has been discovered. But metastasis in mixed tumors seems to have little to do with either malignancy or approaching death for of the 2 cases mentioned, in which it was found in the lymph nodes, 1 patient has remained well for more than 20 years, and the other for more than 5 years. More will be said upon this subject later.

**5 Local interference with function** This is rarely an important occurrence in the clinical behavior of mixed tumors until they have been operated upon. What happens may depend upon the exact location of the tumor. In one position it may prevent the easy movement of the jaw and more and more restrict the opening of the mouth as the tumor becomes larger. In other cases the external auditory meatus may become compressed and unilateral deafness brought about. When the facial nerve or some of its fasciculi are caught in the growing tumor and compressed, facial palsy in varying degrees of severity may result. When branches of the 5th nerve are similarly affected, pain or actual *tic douloureux* may result. In rare cases pressure upon the duct of some part of the gland results in cystic distention.

But when the tumor is operatively attacked, cut into, or only partially removed, local invasive growth may follow with varied results depending upon the extent and magnitude of the invasion.

**6 The general toxic action of absorbed tumor products** It is doubtful whether "tumor products" ever play any part in the pathology of mixed tumors, unless the tumors that ulcerate, bleed and become infected are referred to. Patients with such tumors do not suffer from "tumor products," but from more commonplace conditions—sapremia, septicemia, and similar conditions.

From this analysis and synopsis we are left in some perplexity as to whether mixed tumors are malignant or not. A good deal of this is the result of the terminology used by different pathologists in reporting the tumors and in talking about them. One pathologist



them adenomas, another says "they usually turn out to be adenocarcinomas, a third will find myxomas, chondromas, and sarcomas. How much better it would be to say that they are "mixed tumors" and will probably recur.

Many also assert, as I myself once thought, that they might begin as benign tumors and afterward "become malignant." Were that true, it might be necessary to reverse the thought so as to account for the cases that begin as malignant tumors and later "become benign" as seems to be the case with some of the carcinomatoid tumors.

I have been challenged for my use of the word "carcinomatoid" so I hasten to explain that I use it as a caption under which to place those tumors whose histopathology is in part so suggestive of carcinoma, or so completely that of carcinoma, as to make differentiation impossible. I avoided the already familiar word "carcinoid" because it is the name of a well known tumor of the gastrointestinal apparatus, arising presumably from a type of cell not found in the salivary glands. I do not use it with any pretension to scientific accuracy but as a convenient means of grouping certain remarkable tumors until they are better understood and explained.

The difference between the carcinomas and the carcinomatoids is impressive. In my first paper (18) I gave the criteria by which I believed it possible to recognize the *carcinomas* in these words "When the growth is so rapid as to bring the patient to operation within a year and the excised tissue resembles carcinoma, the prognosis is bad." I am now ready to reiterate the statement, laying down additions as follows: (1) When the pre-operative duration of the tumor is expressed in months, (2) when the tumor grows rapidly, (3) when there is metastasis to the lymph nodes, (4) when the histology of the tumor is that of carcinoma, the tumor usually is carcinoma, and (5) the patient dies within a few years no matter how carefully treated surgically and roentgenologically. That summary applies to more than a dozen cases not included in this paper because they were not mixed tumors. See how different are the facts with reference to the carcinomatoid group of tumors.

The carcinomatoids may so closely resemble carcinomas as to be quite regularly mistaken for them. They may also resemble carcinomas clinically so as to be separated with difficulty from them. I am not always certain myself whether a tumor under consideration is one or the other. But if one has all of the necessary data he will find that between carcinoma and carcinomatoid there are marked differences such as the following:

1. The carcinomatoids usually have an extremely long preoperative duration.

2. They usually appear at an early age. Case 115 first suffered from the tumor at 10 years of age. Case 127 first suffered from the tumor at 4 years of age, and Case 197 has had the tumor since childhood.

3. The course of the tumor growth is very slow. Case 115 had been treated by surgical excision, x-ray and radium treatments for 15 years, and Case 127 had been treated by surgical excisions et cetera, for 25 years.

4. They are almost never metastatic. Case 76 had metastasis in a lymph node that was mistaken for squamous cell carcinoma and Case 115 had "mixed tumor metastasis" in a cervical lymph node.

5. They frequently "recover (?) under treatment. Case 76 after a second excision for a recurrence about 2 years after the first, has seen no sign of recurrence in 20 years. Case 191 after a second operation, has had no recurrence in 18 years and Case 115 after 5 excisions and 2 courses of x-ray treatments, has been free of tumor for 5 years. (She had 3 recurrences and operations for excision after the x-ray treatments had been completed).

#### THE TREATMENT OF MIXED TUMORS

As has already been pointed out the general rule that the best way to treat any tumor is to excise it completely as soon as it is discovered does not apply in the case of mixed tumors. Ordinarily it has everything in its favor for it is easier to remove a very small tumor than a very large one and the resulting scar or disfigurement is much less. But when there is plenty of time to wait and the result of waiting is beneficial it certainly seems wiser not to operate as long as the patient is willing to wait. In most cases the longer he

wants the better, and there is nothing arbitrary about the lemon size that I adopted in compiling the statistics of operation, orange size or grapefruit size might be better except that vascular complications are likely to present themselves when the tumors are very large. Tumors of 6 or 7 pounds have, however, been successfully removed.

It seems useless to attempt to control or modify the growth of the tumor or to postpone its recurrence by the use of x-ray or radium. I have made a special study of the subject and have published a special paper, showing that in not a single case could it be proved that any real benefit has ever been achieved.

Supposed indications for treatment are as follows:

1 The embarrassment of the patient caused by the presence of the disfigurement. This should be overcome by the argument that having already had the tumor for a number of years, it ought not be difficult to endure it a few years longer as its removal may be followed by worse evils such as salivary fistula, which is very rare, facial palsy, which is not rare, or recurrence. That is the sequel to be most dreaded and it will make other operations more difficult.

2 Limitations of the mandibular movement that make opening the mouth difficult. This is a real indication the importance of which cannot be overlooked. It may be well to remove the entire parotid gland in such cases lest there be a recurrence.

3 Pain from pressure upon the sensory nerves. This also may be a perfectly valid reason for operation, and if such treatment is instituted, thorough dissection of the entire gland is to be recommended.

4 Sudden rapid increase in the size of the tumor. Although not always possible to explain, this is usually of no importance. If the tumor is a mixed tumor, rapid growth usually supervenes after the tumor has existed for years. If the tumor is a carcinoma, its excision usually fails to afford much benefit. Every patient with carcinoma of the salivary gland who has come under my observation has died regardless of any kind of treatment, early or late, by excision, radium, or x-ray.

The results of treatment in the case of mixed tumors are impossible to evaluate. In all probability at least one-half of the recurrent cases in my collection were, and a great many still are, believed by their surgeons to have been cured. Doctors fail to follow up their cases, forgetting that 10, 20, 30, or 40 years may pass before a recurrence presents itself.

One case is cited below, to show how necessary persistent follow-up is.

CASE 6, S. H., a white female, aged 23, came to the German (Lankenau) Hospital on February 5, 1910, with a tumor that was known to have been present, at the angle of the left jaw, for 7 years. Its growth had been gradual. The tumor was excised by Dr. John B. Deaver, and upon microscopic examination by various pathologists had been called "myochoondroendothelioma of the neck," "adenocarcinoma of the parotid gland," and "cylindroma." In 1926 in my first paper, "Ninety Tumors of the Parotid Region" (18), I mentioned this case and said "The patient is now living and well after 15 years." Ten years later, in 1936, in my paper "Three Hundred Tumors of the Salivary Glands" (17), I again referred to Case 6 as having remained "without recurrence for 25 years." If any patient can be accepted as cured this should have been true of Case 6, but if you asked me about her present condition, I should be obliged to say that on February 2, 1939, I received a letter in which she said "There seems to be a growth started, just where the other one was. It is about as big as an ox-heart cherry and hurts when I press upon it." This happened 29 years after the operation!

## CONCLUSIONS

The mixed tumors of the salivary glands are a group by themselves. It is impossible to be dogmatic about them for they disregard every canon of oncology and continually do the most unexpected things. It is impossible through the microscopic study of their structure, to foretell what any of them will do. The long delay before any variety may recur. The surgeon and roentgenologist deludes the surgeon and roentgenologist into believing that he has been successful in his treatment, when no good at all has resulted. The same long delay and the occasional recurrence of the tumor 20, 30, or 40 years after operation justifies the question, "Is any patient, once the victim of such a tumor, ever cured?"

It seems appropriate to end where we began and say that the more we learn about the

mixed tumors of the salivary glands, the less we seem to know and "I *ou'd* better not know so much than know so many things that ain't so!"

## REFERENCES

- ARLBERG, H. E. Acta radiol., Stockh., 935, 3-452.
1. BERNHART E B and MICHON J V. Surg. Gyn. Obst., 930, 5-6.
2. BOHRMANN. Erg. allg. Path., 901 vol. 7.
3. CERVASCO. Rev. chir. Par. 909, 47-48.
4. CHIRKOVITZ, H. Ueber das Schleimgewebe in Parathyreoschwüsten. Inaugural Dissertation, Bonn, 812.
5. COMBERG, J. Pathologie, 882, 736.
6. CURRIE and VRAU. Ser. Pathologie bronchiale des tumeurs cervico-faciale etc., Congr. Internat. méd., Paris, 900, section de chir. gen.
7. D. WOOD, E. K., HARVEY W F and LIVER, J R. M. Edinburgh M. J., 935, 45-475.
8. ELLIOTT, E. Beitr. klin. Chir. 906, 3-368.
9. EWING, J. Neoplastic Diseases, 4th ed. p. 21 Philadelphia and London W B. Saunders, 925.
10. FROST and MANSIEAU. Province méd. Par. 906, 8-71.
11. HOOK, J W. Surgery 930, 6-330-334.
12. KROCHENKOW, E. Beitr. path. Anat. 1908, 41-5.
13. LEROUX, ROGER, and LEROUX ROBERT JEAN. Bull. Am. fr. cancer, 934, 3.
14. LEROUX, LEROUX ROBERT, and DELLINGER. Bull. Am. fr. cancer 915.
15. McFARLAND, J. Am. J. M. Sc., 94, 203-207.
16. Idem. Surg. Gyn. Obst., 930, 63-437.
17. Idem. Am. J. M. Sc. 936, 3-842.
18. SCHREIBER, R. F. and MATTICK, W L. Am. J. Roentg. 930, 311.
19. STERN, J. and GERSCHWITZ, C. F. Arch. Surg., 934, 28-203-236.
20. VINCOW R. Die Krankheiten der Halsorgane. Vol. Sechste Auflage. Verlag, p. 302.
21. VOLLMER, Z. C. Deutsch. Zchr. Chir. 915, 4-113.
22. WARTHEN, A. H. Inaugural Dissertation, Strassburg, 880.
23. WOOD F C. Ann. Surg. 904, 30-207.

# AMPUTATIONS FOR ADVANCED ARTERIAL DISEASE

## A Critical Analysis of the Mortality

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THE high mortality from major amputations for arterial disease is frequently attributed to operative delay due to efforts to save the limb by conservative treatment. However, early operation does not seem warranted without first attempting to determine the course of the various factors contributing to the disease by subjecting them to treatment. Not infrequently, patients in whom early amputation seemed advisable have improved under conservative treatment to unexpected recovery. Delay in amputating, however, is not justified when the life of the patient is endangered by complications or when the limb is hopelessly involved by the disease.

This study is an attempt to evaluate the factors contributing to major amputation for advanced vascular disease and to determine whether or not delay in amputating affects the operative mortality.

### MATERIAL STUDIED

During the 7 year period (1935-1941) that has elapsed since the vascular therapy department of the Presbyterian Hospital was organized, 160 patients having complete occlusion of the main artery of 226 lower extremities have been examined and treated. Forty-three of these patients had 50 major amputations (Table I). Those patients who were examined and treated exclusively in the central free dispensary of the Presbyterian Hospital are not included in this study. Within the 7 year period an additional 29 major amputations for vascular disease were performed on patients who were not seen in the department (series II). The *mortality rates* in the 2 series are given in Table I.

All the extremities in series I were found by oscillometric readings to have complete or-

ganic arterial occlusion either at the ankle, knee, or thigh. Dissection of the amputated specimens revealed that oscillometric index up to 0.3 unit may occur in the presence of complete occlusion of the main artery. Accordingly, readings from zero to 0.3 unit were accepted as evidence of complete occlusion of the main artery. (In our experience we have found the results of the oscillometric examination far more accurate than digital palpation of arterial pulsation.)

### FACTORS CONTRIBUTING TO MAJOR AMPUTATION

In reviewing the records of the 50 amputation cases in series I, it is apparent that major operations were definitely indicated. When major amputation is selected the following factors were considered important.

*Pain, infection, gangrene.* The large majority of the amputations were performed for pain, infection, and gangrene in extremities with advanced organic arterial occlusion (Table II). Both pain and gangrene were present in over 80 per cent of the cases and infection in 60 per cent. The lesser incidence of infection may be accounted for by the uncertainty of infection in many cases. Elevation in mouth temperature may not occur or may be very slight because the deficient circulation limits toxic absorption, or, again, moderate elevation in temperature may be due to toxic absorption from gangrenous areas without the presence of infection. Bacteriological studies were not made in all cases. In the series here reported, major amputations were unquestionably necessary as evidenced by the frequency of all 3 complications—pain, infection, and gangrene.

*Site of arterial obstruction.* The level of arterial obstruction in the extremity affects the incidence of amputation. In the senile arteriosclerotic group (Table III), only 18 per cent of the extremities with arterial ob-

From the Rush Medical College of the University of Illinois.  
Read before the Central Surgical Association, February 28,  
1942, Chicago, Illinois.

TABLE I.—INCIDENCE AND HOSPITAL MORTALITY FROM MAJOR AMPUTATIONS FOR ADVANCED ARTERIAL DISEASE

	No. of patients	No. of hospital amputations	Amputations		Mortality	
			No.	Per cent	No.	Per cent
Series I.—From the Vascular Therapy Department, 1932-1941						
Arteriosclerosis						
Bilateral	66	30	29	30		
Unilateral	37	37		33	16	6.1
Thromboangiitis obliterans	23	15 <sup>a</sup>	1	4		
Emboli and thromboemboli	13	14		10		6.6
Popliteal tumor (no aneurysm)				100		
Total	140	126	30	22		

Series II. Not examined in Vascular Therapy Department, 1932-1941

Total			29		6	10
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\*Five additional amputations were amputated elsewhere prior to patients' coming under our care with points involvement of remaining lower extremity. After amputations was performed elsewhere after the third procedure, when we refused further treatment due to patient's uncooperative attitude. (Both deaths followed the second major amputation. One case reported.)

TABLE II.—INDICATIONS FOR MAJOR AMPUTATIONS FOR ADVANCED ARTERIAL DISEASE

	Indications for amputation			Average age		
	Pain Per cent	Infection Per cent	Gangrene Per cent	All cases	Amputation cases	Amputation on hospital death
Arteriosclerosis						
Bilateral	3	66	73.3	66		36
Unilateral	64		86	57	65	26
Thromboangiitis obliterans	100	100	100	46	36	
Emboli and thromboemboli	100	100	100		47	
Popliteal tumor (no aneurysm)	100		50	75	75	

TABLE III.—INCIDENCE OF AMPUTATION ACCORDING TO LEVEL OF COMPLETE OBSTRUCTION IN THE MAIN ARTERY

	Above Knee		Below Knee		Foot		Total	
	No. cases	Per cent of amputations	No. cases	Per cent of amputations	No. cases	Per cent of amputations	No. cases	Per cent of amputations
Arteriosclerosis								
Bilateral	43	18	30	60				30.6
Unilateral		47		64		100	29	26
Thromboangiitis obliterans	26	6.6	16			49	37	
Emboli and thromboemboli			16					
Popliteal tumor (no aneurysm)					100			100
Total	69	30.3	29	12.3	44	47		

struction at the ankle were amputated while more than 50 per cent required amputation when the occlusion was at a higher level. It is apparent, therefore, that conservative treatment is more successful when the arterial obstruction is confined to the ankle or foot.

In the diabetic patient the incidence of amputation was very high (50 per cent) irrespective of the level of occlusion in the main artery. When amputation is being considered the presence of extensive arterial occlusion makes it very unlikely that conservative treat-

ment will improve the condition and therefore major operation should not be unduly delayed. This report, however, does not include the majority of diabetic patients who have only peripheral arteriolar involvement. In the absence of main artery occlusion these patients have been treated successfully by conservative measures and minor surgical procedures.

The frequency of major amputations for high arterial occlusion for embolism was less than that observed when the occlusion was at a lower level. This is due to the presence of greater collateral circulation at the higher level. However, when the main artery is extensively occluded by secondary propagating thromboses there is little hope of saving the limb by conservative treatment. This fact should be given serious consideration when there is a tendency to delay operation.

*Age as a factor.* Advanced age in a patient does not justify continuance of conservative treatment when amputation is otherwise indicated. In those cases studied, the average age of 66 patients having senile arteriosclerotic vascular disease was 68 years, of these patients, 19 underwent major amputation. The average age in this group was 71 years and, of the 4 deaths that ensued only 1 patient was under 79 years (Table II), which fact further indicates that the patient's physiological age is a more important factor than his actual age in considering amputation.

In the other groups studied, age as a factor in deciding upon operation was of less importance. In all cases, however, patients of advanced age suffering with extensive arterial occlusion are much less likely to benefit by conservative treatment. The incidence of amputation among the arteriosclerotic patients was particularly high, as was the mortality (Table I). However, the risk in not operating upon these patients is even greater than that taken in operating.

*Bilateral involvement of extremities.* There is a greater tendency to delay amputation when both extremities are involved or when one extremity has already been amputated. Consequently, amputation of the second limb would be expected to involve a higher mortality. Five bilateral amputations for arterio-

sclerotic gangrene (7 of 44 cases of bilateral involvement required amputations) were successfully performed. Two deaths followed the second major amputation for diabetic arteriosclerosis and were due to coronary thrombosis and pulmonary embolism, respectively. These results do not support the contention that operative delay contributes to the mortality from amputations (2).

#### HOSPITAL MORTALITY FOLLOWING AMPUTATIONS

The 6 deaths from major amputations occurred among those patients having extensive arteriosclerosis (Table I). These operations involve the same hazard as other major operations performed upon patients with arteriosclerosis due to advanced age or to diabetes mellitus. Of the 6 deaths which occurred in the series of 50 amputations, 3 were probably contributed to by errors in surgical judgment.

*Type of operation.* Except for 1 upper leg amputation, all operations were performed at the supracondylar or midhigh level. Only 1 major reamputation was necessary (Case 1). No guillotine operation was performed. In the presence of advanced organic arterial occlusion there should be no compromising on the level for amputation. Two of the deaths followed major amputations which were resorted to after less radical surgery had failed to give relief. Depending upon the surgeon's judgment, wound nonclosure or closure was used, with or without drainage.

*Surgical and medical care.* The surgery was performed by 14 members of the surgical staff. One hospital death occurred on 6 surgical services. The medical care was provided by various members of the medical staff. Diabetic management is largely standardized by the diabetic service which may be said to account for the excellent convalescence of the diabetic patients and for the absence of deaths from diabetic coma or from wound infection (series I).

*Anesthesia.* With 2 exceptions all major operations were performed under ethylene anesthesia. The 2 patients mentioned were operated upon under local infiltrating and block anesthesia.

## CASE REPORTS OF HOSPITAL DEATHS

*Senile arteriosclerosis*

**CASE 1.** Mr C. C., aged 70 years, was admitted March 8, 1935 suffering with gangrene of left first toe. Oscillometric readings revealed complete or gangic arterial occlusion at the ankle. He remained in the hospital 17 days. Fifty hours of pavyx treatments were given and the condition of the toe and foot improved. On April 9, 1935 he was readmitted to the hospital for acute urinary retention for which electrosection of the prostate was performed. He was discharged from the hospital May 9 1935.

He was readmitted to the hospital July 10, 1935, with recurrence of pain and gangrene of the toe of 1 month's duration. On July 23, 1935, the toe was amputated and because of the absence of bleeding midleg amputation was then performed. The midleg stump failed to heal and on September 5, 1935, a midhigh amputation was performed. Infection of the gangrenous stump continued until death from bronchopneumonia occurred on October 22 1935.

**CASE 2.** Mr O. T. aged 80 years, was admitted September 1, 1936, for infected gangrene of the left first toe and foot. Because of the advanced arterial occlusion and infection of the foot which had been present for 3 months prior to examination, midhigh amputation was advised and performed the day following admission. Right pulmonary atelectasis followed operation and the patient died the 12th postoperative day from bronchopneumonia.

**CASE 3.** Mr A. M. aged 75 years, had been ill health for more than 10 years and suffered with circulatory symptoms of the lower extremities for 8 years prior to his admission October 3 1930. Daily treatments of alternating negative pressure but no positive pressure were given for 7 days when an extension of the infection was noted with mouth temperature of 100 degrees F.

Midhigh amputation was then performed. The wound was closed without drainage as is recommended in some reports in the literature. In this instance, however because of the infection present, the surgical decision to close the wound without drainage was illadvised.

The day following amputation the patient's temperature rose from 90 to 103 degrees F and his condition became progressively worse. The next day the sutures were removed and a large amount of old clotted blood was evacuated. Bacteriological studies revealed mixed infection with anaerobes, probably *Bacillus welchii* (milk fermentation not typical). He died on the 3d postoperative day from gas bacil infection (*Bacillus welchii*) of the amputation stump thigh abdominal wall, scrotum, left psoas muscle and mesentery of the small bowel.

**CASE 4.** Mr J. E. aged 80 years was admitted September 9, 1940, suffering with gangrene of the left 4th and 5th toes and advanced organic arterial disease. Oscillometric readings revealed complete occlusion of the main arteries of the knee. Although the toes appeared infected, only an occasional mouth temperature of 99 degrees F was recorded. Twenty

one hours of treatment with alternating negative pressure but no positive pressure were cautiously given but the condition failed to improve and the 2 toes became more involved in the gangrenous process. Despite the evidence of infection, amputation of the 4th and 5th toes was performed under local infiltrating anesthesia. The mouth temperature almost immediately became elevated to 101 degrees F. The infection spread rapidly and the pain increased.

Four days after the toes were amputated, midhigh amputation was performed under local anesthesia. The wound was closed without drainage. The stump rapidly became gangrenous and infected, and the mouth temperature remained elevated. The patient's general condition became progressively worse and he died on the 32d postoperative day from a cerebral accident.

Three of the 4 deaths followed serious infection of the operative wound. Two of these had initial minor amputations through areas of infected gangrene of the toes although neither had a febrile course. The third death followed gas gangrene infection in which case a large hematoma was evacuated the 2d day after closure of the wound without drainage. These observations emphasize the danger of local amputations in the presence of advanced organic arterial disease and of nondrainage of wounds following amputation for infected gangrene.

*Diabetic arteriosclerosis*

**CASE 5.** Mrs. S., aged 61 years, was admitted October 1935 suffering with advanced bilateral diabetic vascular disease. Oscillometric readings revealed complete occlusion of the femoral arteries. She remained in the hospital for 6 days during which time large painful infarcts of both heels failed to respond to pavyx treatments. The patient was readmitted January 1936. Left midhigh amputation was performed February 24 1936, with recovery and discharge from the hospital on March 3 1936.

On September 10, 1936 she resumed pavyx treatments because of continuous pain in the right leg and foot. Complete relief from pain occurred during treatment. There was no infection present. Because of her inability to continue treatments she requested the second midhigh amputation. This was performed September 29, 1936. Sudden death from pulmonary embolism occurred October 3 1936.

**CASE 6.** Mr G. aged 58 years, as admitted January 9, 1936, suffering with bilateral diabetic vascular disease. Thirteen hours of pavyx treatment were given. Because of the continuous rest pain in the right foot, supracondylar amputation was performed January 16 1936. He was discharged from the hospital February 1936, and returned

April 17, 1936, for periodic pavaex treatments of the left leg until March, 1937. Marked improvement in the condition of the leg and foot followed the treatments.

Sixteen months later, on July 31, 1938, he returned to the hospital with recurrence of pain in the left foot. Nine months previously he had been confined to bed for 6 weeks with cardiac decompensation. On admission the first toe was red and inflamed. No pavaex treatments were given because of spreading gangrene and severe diabetes. Mid thigh amputation was performed August 16, 1938. Cardiac decompensation and pulmonary edema followed operation and the patient died August 20, 1938.

Neither of the 2 deaths following the second major amputation for diabetic gangrene can be attributed to delay in operating because of attempts to save the limb by conservative treatment. Both individuals were suffering with far advanced arteriosclerosis and had previously undergone successful major amputation of the other extremity.

#### EVALUATION

Major amputation for advanced arterial disease is definitely indicated when a limb cannot be saved by conservative treatment or when the life of the patient is endangered by serious complications. In the 50 amputations (series I) under the advisement of the vascular therapy department the mortality rate of 12 per cent is especially favorable in view of the extensive use of conservative treatment and the fact that the operations were performed on 14 surgical services. During the same period 29 extremities which were not seen in the department were amputated with a mortality rate of 20.7 per cent. These results do not confirm the contention of de Takats and Reynolds, Veal, and others (1), that operative delay due to conservative treatment contributes to the mortality rate from amputations.

Although the series herewith reported is not as large as those reported elsewhere, the 50 amputations occurred in a series of 226 extremities with main artery occlusion. Despite the fact that amputations were delayed and the operations were not performed by a special surgical service, the hospital mortality in the various classifications of advanced arterial disease compares very favorably with the reports from specialized services elsewhere. Williams and O'Kane were able to

reduce their mortality rate from 85 per cent in 1931 to 36 per cent in 1935 after amputation cases were concentrated on one surgical and one medical service. McKittrick's series (5, 6, 7) of 496 amputations had a mortality rate of 14 per cent and Veal's series of 171 amputations had a mortality rate of 39.1 per cent. From the University of Pennsylvania Hospital, Eliason reported 83 major amputations with a 25 per cent mortality rate from amputation for diabetic gangrene. These mortality rates are higher than should be expected on specialized services with large series.

In order to lower the mortality rate from amputation it is advisable to study the causes of the operative deaths. More emphasis should be placed on the surgical judgment that is used in the individual case than on the number of amputation cases. Three of the 6 deaths herewith reported were probably contributed to by errors in surgical judgment as when minor amputations preceded major amputation and nondrainage of a closed wound resulted in serious infections of the stumps. Experienced surgical judgment is especially needed in deciding upon wound closure or nonclosure and drainage or nondrainage. McKittrick with his extensive experience advises either a guillotine operation for infected gangrene or wound closure without drainage while Eliason recommends closure with drainage. Faxon and Taylor (9, 10) both advise against draining for primary closed amputations. It is not possible for the less experienced surgeon to appraise individual cases. In the series reported the largest number on one surgical service was 17 major amputations with 1 death (mortality, 5.5 per cent), nonclosure or closure with a small gutta-percha drain was used for a few days in almost all the cases. In general, it is safer when major amputation is done for infected gangrene that the operative wound be drained for a few days to assure evacuation of blood or primary wound secretion.

The actual age of the patient should not be an important contraindication for major amputation. Because of the advanced age of some patients there is a risk in operating, but the risk is greater when amputation is not done to relieve unnecessary suffering or to



save the life of the patient. The operative risk of this operation should not be greater than that for other major operations upon patients of advanced age.

#### CONCLUSIONS

Operative delay due to efforts to save the limb by nonoperative treatment did not contribute to the mortality in the 50 major amputations for advanced arterial disease herein discussed. Despite the extensive use of conservative treatment the mortality rate in these cases is the lowest thus far recorded.

In the presence of extensive organic arterial occlusion, minor amputations are usually unsuccessful and increase the risk incurred in secondary major amputation.

Nondrainage of closed amputation wounds may prove dangerous and is especially ill advised when there is a possibility of gas bacillus infection.

The operative risk involved in major amputation should not be greater than that for other major operations performed upon patients of advanced age with extensive arteriosclerosis.

#### REFERENCES

- APPELBAUM, G. and L. HANCOCK M. J. 1929, 51: 357-357.
1. DE TAKATS, G., and REYNOLDS, J. T. Arch. Surg. 1930, 40: 55-57.
2. ELLMAN, E. L., ELLI, W. H. GILBERT, F. D. Surg. Gyn. Obst., 1937, 64: 1005-1014.
3. FARRAR, H. H. J. Am. M. Ass. 1930, 5: 98-103.
4. McKENZIE, Leland S., and FRITZ, T. C. Am. Surg. 1934, 100: 655-655.
5. Idem. J. Am. M. Ass., 1935, 3: 1213-1217.
6. Idem. Arch. Surg. 1940, 40: 351-361.
7. SMITH, B. C. Surgery 1937, 500-516.
8. TAYLOR, FREDERICK W. J. Am. M. Ass. 1935, 1: 96-100.
9. Idem. Surg. Gyn. Obst. 1935, 67: 1-17.
10. VIAL, J. R., and McSTERNON, L. M. Surg. Gyn. Obst., 1935, 60: 840-847.
11. WILCOX, L. E., and CLARKE, O. T. Proc. Wyo. Clin. 1934, 16: 795-800.
12. WILLIAMS, FREDERICK W. and O'KANE, THOMAS J. Surg. Gyn. Obst., 1937, 64: 956-963.

# A METHOD FOR OBTAINING AINOGRAMS OF THE VEINS OF THE EXTREMITIES

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**R**ADIOGRAPHIC AINOGRAMS of the deep veins of the extremities by the method described herein are an extremely popular means to the physician for establishing a diagnosis of deep vein thrombosis. The procedure is simple and safe and the deep vein system may be visualized in a few minutes. The patient is not inconvenienced in any way.

Before the technic described here is attempted, the patient must be in a supine position with the extremity to be examined extended. It is important to observe the patient's external physical characteristics before attempting to cannulate the vein. If the external physical characteristics of the extremity are such as to make it difficult to locate the vein, the method proposed in this article for determining the deep vein system is performed first.

1. The patient is on the x-ray table on which the plate is to be made.

2. With the leg dependent over the edge of the table, a large needle is inserted into a vein on the dorsum of the foot or on the ankle, one of the tributaries of the internal saphenous system. The course of the internal saphenous is inferior to the internal malleolus and it is relatively superficial usually permitting the insertion of a needle without an incision.

3. The tubing of an infusion set containing normal salt solution is connected with the needle. The infusion is permitted to drip relatively rapidly.

4. The needle is then strapped securely in position with adhesive and the patient rotates and lies down on the table.

5. A large cassette containing the films is placed behind the calf and thigh (Fig. 1). The leg is slightly externally rotated.

6. A very flexible tourniquet is applied around the leg usually at the junction of the middle and lower thirds, sufficiently tight to supplant circulation in the superficial vein. This is done so that the infusion from the vein will flow into the deep system.

7. A syringe containing air is used to remove the distal part of a vacuum cupped syringe. The vacuum container or distal part is placed directly against the tubing of the needle and the needle.

8. The air is drawn out and the exposure is delayed three to five minutes.

9. After the exposure the infusion continues to run for several minutes in order to wash the distal part of the veins.

10. It is possible to rotate the leg and get a lateral or oblique view after the plate is replaced. The same one or other desired view may be placed by her under the thigh and the femoral vein exposed.

As to the radiation of the deep veins may be obtained by this method is demonstrated in the accompanying roentgenograms.

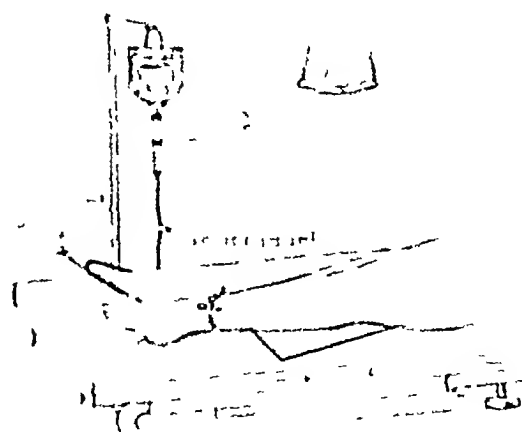


Fig. 1. Dorsal view illustrating the method of hunting for the femoral vein from superficial into the deep vein system by use of a tourniquet around the leg. The steps in the procedure are described in the text.



Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 2. Anteroposterior and lateral venograms in leg in which the internal saphenous system is obstructed by recent thrombosis near the knee (see arrow). The infusion is running into superficial vein of the foot, tributary of the internal saphenous system. A tourniquet is used. The diodrast is seen in the saphenous up to the point of thrombosis as is indicated by the arrow. The diodrast is also shunted into the deep system which is filled and found to be normal. A P T indicates anterior and posterior tibial.

Fig. 3. Venogram showing failure to disclose any of the deep veins when tourniquet is placed around thigh just above knee and contrast media is injected into superficial vein of foot. The diodrast in this instance is not shunted into the deep system. I S Internal saphenous.

Fig. 4. Anteroposterior and lateral roentgenograms of the leg. The veins are visualized by diodrast. A needle is inserted into vein on the dorsum of the foot, and tourniquet, arrow, around the junction of the middle and lower thirds of the leg shunted the blood into the deep system. The venous system is adequately exposed showing posterior tibial and anterior tibial veins and their junction

above the interosseous membrane (forms the popliteal). Several arteries are disclosed. The venous system looks normal. E S, External saphenous. Compare this venogram with the blocked deep system on the opposite leg of the same patient shown in Figure 5.

Fig. 5. The left leg of the patient, lower right leg shown in Figure 4, had long standing edema from obstruction of the deep venous system. This resulted from fracture of the femur 6 years ago. The arrow indicates the tourniquet which is applied at the junction of the middle and lower thirds of the leg. Diodrast may be seen in the superficial system below and above the tourniquet and some veins of the deep system below it. Although a low forced it is up the superficial system and may be seen in the internal saphenous vein. I S of the thigh, none of the deep veins are visualized. A control venogram of the right leg (Fig. 4) had as normal showed visualization of the deep veins under the same circumstances. The tourniquet applied at the junction of the middle and lower thirds of the leg shunted the contrast media into the deep system. A T Anterior tibial.

I have attempted to obtain venograms of the deep system by injecting diodrast into the superficial veins of the foot without the use of the tourniquet to shunt the media into the deep system. This, however has not been uniformly successful because the diodrast usually goes up the superficial system and does not always expose the deep system. Moreover if the tourniquet is placed high around the thigh, the contrast media is not promptly shunted into the deep system and the deep veins will not be visualized.

Though the superficial system may not be exposed well by this particular method super-

ficial thromboses are usually evident on clinical examination.

Finally a word of caution should be expressed concerning venography. More extensive thrombosis (4) and even death (5) have been reported as complications.

#### REFERENCES

1. BARTER, G. Acta chirurgica (supp. 6) 1937, 24.  
Quoted by SARRY, FRANK, and STILES (3).
2. DOUGHERTY, J. and HOWARD, J. Surg. Gyn. Obst., 94: 7, 1957.
3. GOLDBERG, H. L. and BARTER, S. J. Am. M. Ass., 94: 9, 1957.
4. HOWARD, J. J. Am. M. Ass., 94: 9, 1957.
5. HARRIS, A. FRAZER, H. and STUART, J. J. Am. M. Ass., 94: 9, 1957.

# THE CARBON DIOXIDE SNOW-ELECTROCAUTERY TECHNIQUE FOR OCCLUSION OF LARGE VEINS

Suggested Application to Venous Angioma of the Brain

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**A**NALW technique for the occlusion of large venous channels for use when conventional methods are not adequate, has been developed. The details of this procedure, and its possible application in neurosurgery, will be considered.

This work was begun in the hope of finding an effective treatment for venous angioma of the brain which is thought to be a congenital blood vessel malformation rather than a new-growth. There are simple serpentine and racemose types. The simple type consists of a hugely dilated single vein, the serpentine of a group of enlarged vessels lying superficially, and the racemose of a mass of distended veins which lies on the surface and extends deeply into the substance of the brain replacing nervous tissue. On the surface the serpentine and racemose types look much alike and cannot be distinguished. Angiomatous vessels are very thin walled and fragile. Occasionally, thick but brittle walls are seen as the result of hyaline change.

Treatment has included surgery and x-ray therapy. The principal danger in the surgical approach to this lesion is severe bleeding from extremely large and fragile vessels, at times uncontrollable. The ligature and the electrocautery have been used with very little success. At operation these lesions, for the most part, have been simply exposed without attempt at removal or obliteration. This occurred in the cases presented by Spiller, Dandy, and Brock and Dyke. Others have attempted removal with severe, and sometimes fatal, hemorrhage resulting, as reported by v. Bergmann, Krause, Worster-Drought

and Ballmer, Perthes, and Cushing and Bailey. Radiation therapy has also been attempted on these vascular masses, but the results have not been encouraging.

Various ways of obliterating large vessels were therefore considered, and finally an effective technique was developed, which involves the combined use of carbon dioxide snow and the electrocautery. Application of the electrocautery alone to a large vein almost always results in a tear. The heat produced is not sufficient to coagulate the vessel walls and the blood stream, the major effect of the cautery is then exerted on the proximal wall, which tears. Therefore, temporary emptying of the vessel, eliminating the interposed blood stream, would be desirable to permit coagulation of the apposed walls. Carbon dioxide snow applied with moderate pressure empties the lumen, by forcing the blood out of the strip, and freezes the vessel, the electrocautery may then be applied and the vein occluded. This procedure may perhaps be of use in the treatment of venous angioma of the brain.

## EQUIPMENT

Carbon dioxide snow, or dry ice, is a widely used refrigerant, which has a temperature of  $-78$  degrees C. It is easily obtained from distributors of dry ice and ice cream, and may be kept in vacuum jars, in which there is a loss of 5 per cent per day. A film of gas surrounds the material, acting as an insulator, and must be removed by pressure before freezing can take place. Pressure of carbon dioxide snow against tissues causes immediate freezing of the area in direct contact with it. The rate and depth of freezing depend upon the pressure exerted, conduction of heat from below extends the freezing to greater depths.

From the Department of Neurology, Columbia University College of Physicians and Surgeons and the Neurological Institute of New York. Work carried out in laboratory of Dr. Tracy J. Putnam.

Dry ice is bacteriologically sterile. Repeated efforts to grow organisms on agar blood agar broth and anaerobic meat broth culture have failed.

It can be cut into desired shapes with a hack saw. A block of the freezing agent is placed into a wooden frame with slots at intervals to guide the saw. There is an overlapping border on the sides by means of which the device is clamped to a table. The cut pieces in these experiments measured 6 by 2 by 2 centimeters. Smaller sections are best cut with a hammer and moderately keen edged knife.

A curved clamp was found best for grasping and applying the carbon dioxide snow. When dry ice is held in a steel instrument, the metal becomes cold and condensed water vapor which immediately freezes, is deposited on the prongs. This frost causes the instrument to adhere to moist gauze and tissues. To prevent this, the prongs of the instrument are covered with close fitting rubber tubing.

Both spark-gap and vacuum tube electrocauteries were employed in these experiments. The spark-gap machine was the Liebel Flaksheim portable Boyle electrosurgical unit which operates at approximately 800,000 cycles per second and has a wave train frequency of 7,000 per second. The vacuum tube apparatus was the Cameron cauteradio model O a small portable machine which operates at 5,000,000 oscillations per second. The ball electrode measuring 5 millimeters in diameter was used on the vessels.

#### TECHNIQUE

This procedure has been used successfully on the inferior vena cava of cats between the renal and iliac vessels in more than 50 experiments. The vessel of an average diameter of 6 millimeters, was exposed by a lower abdominal midline incision, retraction cephalad of the small bowel, and dissection through the peritoneum.

When a block of dry ice is applied to a segment of blood vessel with moderate pressure for one minute and then removed, the vessel is seen to be covered with frost. It contains no blood and is cold and hard on palpation. At the end of about one minute blood appears

at each end of the frozen strip. The two columns slowly move toward the middle where they join and normal blood flow is resumed. The vessel being undamaged, then appears exactly as it did before freezing. Pressure is an important factor both in emptying and freezing a vascular channel. Application of carbon dioxide snow without pressure leaves the vessel unfrozen with blood in the lumen.

To occlude a segment of vein a block of dry ice is applied to it with moderate pressure. This also freezes lateral tributaries for a short distance before they enter the vessel. A larger strip is frozen than is to be coagulated, for example freezing 6 centimeters and coagulating the middle 3 centimeters. After one minute the refrigerant is removed and the electrocautery is applied. The frozen extremities and tributaries are watched. If blood enters them, electrocoagulation is stopped, and the procedure is repeated.

So long as the extremities and the lateral tributaries are frozen the strip usually remains flat and bloodless during coagulation. If, however, blood appears in the lumen, coagulation is stopped. The ends are thawed, and the procedure is repeated.

The presence of blood in the frozen strip may be accounted for in a number of ways. (1) The vessel may have been incompletely emptied because of insufficient pressure in the application of the refrigerant. (2) The blood may have entered through deep tributaries. The presence of very small quantities of blood does not offer much hindrance to effective coagulation. Deep tributaries in these experiments have caused no difficulty. If the deep tributaries of a vein were very large it might be possible gradually to occlude the vessel by repeating the procedure several times, stopping when blood appeared in the lumen.

In coagulation the objective is occlusion with a minimum of damage to the vessel wall. Although it would be best to obliterate the lumen with no carbonization of tissue low intensities of current frequently coagulate only a part of the wall without occlusion. Therefore a current of moderate strength has been used resulting in slight carbonization of the anterior wall. It is difficult to know exactly how much current is delivered at each

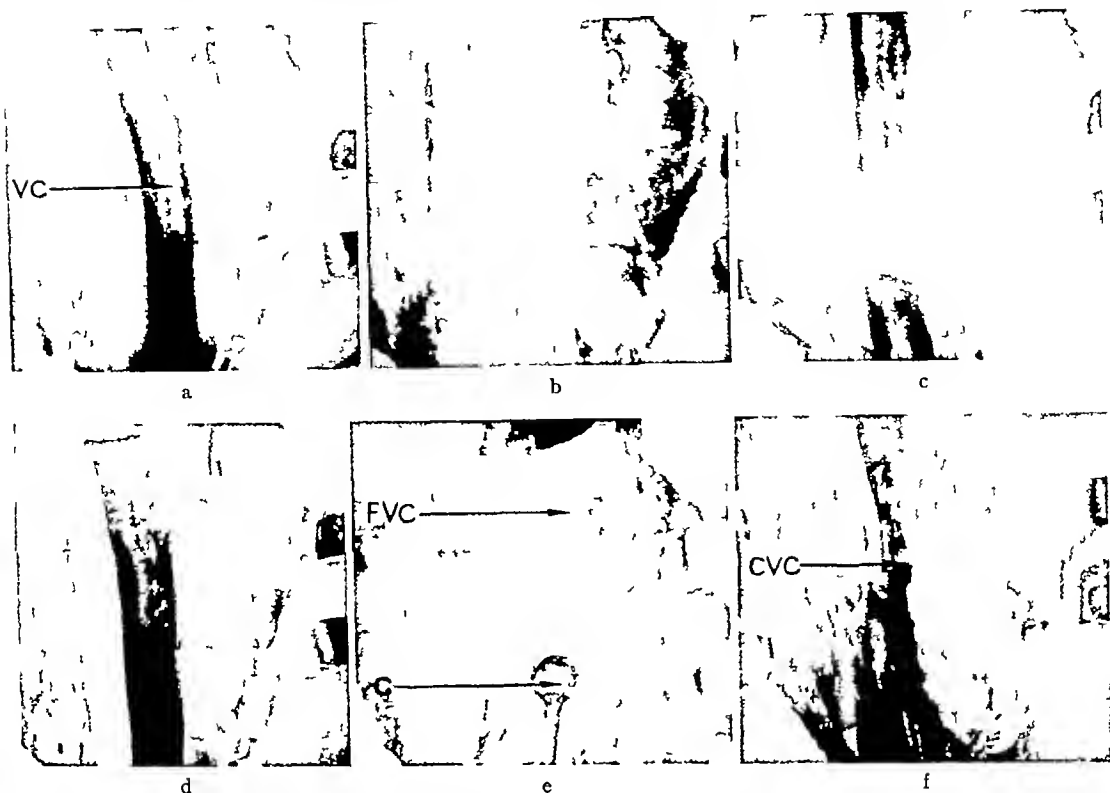


Fig 1 Cat inferior vena cava, 6 millimeters in diameter which was frozen and thawed, and then frozen again and electrocoagulated a, Normal VC, Inferior vena cava b, Frozen c, Thawing d, Thawed e, Application of

electrocautery to refrozen vessel FVC, Frozen segment of the inferior vena cava C, Electrocautery f Coagulated. CVC, indicates the coagulated segment of the inferior vena cava

setting of the current control In these experiments the control has been set at 2.5 in the vacuum tube machine and at 30-35 in the spark-gap electrocautery The ball electrode is moved rapidly back and forth over the center of the frozen strip, in order to cover the area and to distribute the current uniformly The procedure is continued until coagulation and a slight degree of carbonization of tissue have occurred At this point, the vessel is usually occluded The frozen ends are then allowed to thaw If the lumen is not completely obliterated, the vessel is refrozen and again coagulated To occlude additional strips, the procedure is repeated

After one segment has been occluded, the portion of the vessel proximal to it is even more easily emptied by freezing with moderate pressure (allowing the dry ice to overlap a short distance on the coagulated portion)

as the main source of supply has been cut off and blood is being moved in the direction of flow Slightly more difficulty may be encountered in emptying strips distal to the coagulated segment, because blood is being moved against the venous current Nevertheless, it is almost always accomplished by the application of dry ice with pressure in the usual manner, allowing the refrigerant to overlap slightly on the occluded strip is of help If this is not effective, one end of the block of carbon dioxide snow is placed on the near part of the coagulated segment The piece is then lowered until its whole undersurface is in contact with the vessel Pressure is applied as it is moved into position By these methods, additional portions of the vessel may be emptied and then coagulated

If cauterization is carried too far or is continued in spite of the presence of blood in the



Fig. 2. Bleeding cat inferior vena cava, 6 millimeters in diameter frozen, and thawed to demonstrate site of tear and then frozen and coagulated. a, Bleeding VC. b, Frozen VC. c, Thawing. d, Thawed segment of the inferior vena cava. e, Thawed segment of the inferior vena cava.

VC, Inferior vena cava. A, Abdominal aorta. b, Frozen VC. c, Thawing. d, Thawed segment of the inferior vena cava. e, Thawed segment of the inferior vena cava.

lumen the vessel may tear. In that event, the strip is refrozen and the area about the tear is coagulated. When the location of the tear is not known the vessel is frozen for 15 seconds and then allowed to thaw until blood oozes from the opening. When the laceration has been identified the segment about it is then refrozen in the usual manner and coagulated. Free blood is frozen by the dry ice and unless excessive does not interfere with the procedure. If much blood is present it may be removed by suction while the dry ice is in place. This procedure has been used more than twenty times on the purposely torn inferior vena cava of cats, without failure.

In short, to occlude a segment of vein a block of carbon dioxide snow is applied to it with moderate pressure. After one minute the refrigerant is removed. The electrocautery is

passed back and forth over the vessel, until coagulation and a slight degree of carbonization have occurred.

In order successfully to occlude venous channels, or permanently control bleeding from them by the use of the carbon dioxide snow-electrocautery technique the vessels must be emptied of blood. The procedure may therefore be used only on veins in their long axes. When only the cross-section of a blood vessel presents itself a may be the case after excision of a block of cortical tissue, bleeding cannot be permanently controlled in this manner.

The widest vessel occluded by use of this technique was a dog inferior vena cava, 13 millimeters in diameter. In so far as length is concerned a vein of any extent may be obliterated by freezing and coagulating con-

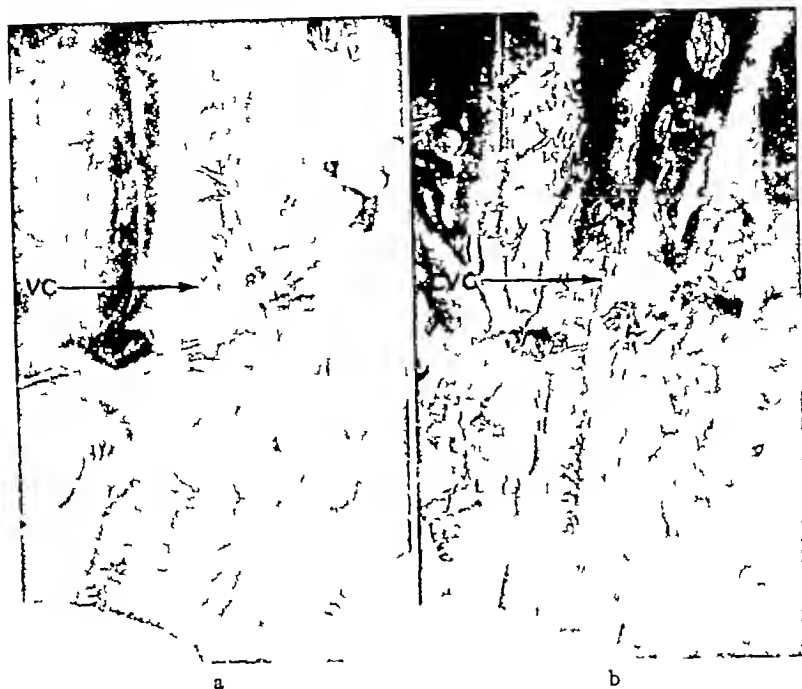


Fig 3 Dog inferior vena cava, 13 millimeters in diameter, frozen and coagulated  
a, Normal VC, Inferior vena cava b, Coagulated CVC, Coagulated segment of the  
inferior vena cava.

secutive strips Work is in progress to develop a similar technique for the occlusion of arteries, for possible use in the treatment of arteriovenous angioma of the brain

#### CONSIDERATION OF LOW TEMPERATURE FREEZING

In 1938 Jahnel reported his work on the freezing of spermatozoa at extremely low temperatures Specimens were maintained at  $-196$  degrees C in liquid nitrogen for 52 hours On thawing, a considerable number of normal, motile cells was seen Another specimen was kept at  $-79$  degrees C in a mixture of carbon dioxide snow and alcohol for 40 days, with the same result Surprisingly, at temperatures nearer the freezing point of water,  $-10$  degrees C and  $-20$  degrees C, very few normal cells were visible on thawing

Several theories have been advanced to explain why freezing at very low temperatures does so little damage to cells as compared to that done by freezing at temperatures just below 0 degrees C Richardson and Scherubel

studied cells under the microscope during freezing and observed that at temperatures just below the freezing point of water, ice formed in the extracellular spaces sooner than it did intracellularly, and water was extracted from the cell Damage may result from the mechanical compression of the cell, or from an increased concentration of toxic substances within it Plank, Ehrenbaum, and Reuter demonstrated that the rate of freezing was important, since, in tissues frozen quickly at very low temperatures, ice formed within and without the cells simultaneously without the passage of water Mechanical compression and increased concentration of toxic substances are both avoided

A somewhat different explanation is offered by the researches of Moran and Hardy Working with colloids they showed that, in slow freezing, crystallization progressed from few centers with the formation of large crystals which distorted the normal architecture of the colloid In rapid freezing, crystallization proceeded from many centers, the crys-



tals were much smaller and the structure of the colloid was preserved.

These theories offer possible explanations of why low temperature freezing does little damage at the time of refrigeration. Maintenance in a frozen state for long periods of time without injury probably depends on the cessation or diminution of metabolic activity. If cell material is not consumed at all or is expended only in small quantities there is little need for elimination or replenishment. This phase of the problem has not as yet been completely worked out.

Jahnel's findings on the low temperature freezing of spermatozoa have been duplicated in living brain tissue. Koskoff and associates have reported a method of removing blocks of brain tissue after *in situ* refrigeration with liquid nitrogen, which has a temperature of  $-196$  degrees C. An instrument which they have devised is inserted into the brain. Liquid nitrogen is then poured into it and after 1 minute a core of frozen tissue is delivered. Microscopic examination of the excised block revealed normal cortical architecture. Study of the area adjacent to the crater disclosed small hemorrhages but intact cell structure. These findings indicate that freezing at very low temperatures does not injure brain tissue.

It is of interest that other investigators, including Astapow and Bobkow, Speransky and Nims and associates, have reported considerable damage following freezing of the brains of experimental animals. The freezing agents used were carbon dioxide gas and a mixture of carbon dioxide snow and ether; these were applied not directly but in metal containers. Very cold metal surfaces adhere to moist tissues and are separated with much difficulty, whereas blocks of dry ice are easily removed. In the instrument devised for refrigeration with carbon dioxide gas, the gas is transmitted through a tube into a metal chamber which is applied to the cortex. Fedoroff in describing the removal of the apparatus from the frozen cortex, has said:

Particular difficulties are found in the dosage of the freezing as the freezing apparatus can not be separated from the hard surface of the brain after thawing. The dura and the brain are usually torn during the removal.

It can be successfully separated by striking extremely sharp blows on one or more surfaces of the tube of the instrument. It seems not unlikely that mechanical trauma has played a considerable part in the damage resulting from this type of refrigeration.

There is also an element of mechanical trauma though considerably less, in freezing with blocks of dry ice, as the refrigerant must be applied with moderate pressure for the reasons mentioned. Therefore, in evaluating the pathological effects of freezing with blocks of dry ice the part played by pressure must be considered.

A 1 centimeter strip of the inferior vena cava of a cat was frozen with a block of carbon dioxide snow applied with moderate pressure for 1 minute. In order to study the results of low temperature freezing of vascular tissue, Examination 3 weeks later disclosed that the vessel was patent and that there was no sterile abscess or infection. Microscopic examination showed the vessel to be of normal appearance. A slight separation of the fibers of the outer layer of the adventitia was the only change seen. These findings might have been expected from what is known of low temperature freezing and indicate that vascular tissue can tolerate the pressure necessary to empty and freeze a blood vessel.

In order to study the effects of freezing brain tissue with blocks of carbon dioxide snow the brains of 5 cats were exposed and dry ice was applied with moderate pressure. The freezing agent was placed on an area of cortex behind the motor strip for 1 minute. Pressure was tolerated with very little displacement of brain tissue. No change in vital signs was noted during the period of freezing nor did convulsive movements appear. After the dry ice was removed a frost was seen over the frozen area, which thawed within 1 minute. The thawed surface had a faintly bluish tinge and the vessels were dilated surrounding areas showed no change. The motor strip was frozen in the same manner without convulsions. To have some idea of the damage caused by pressure alone a piece of plastic material of the same size as the block of dry ice was placed with moderate pressure on a similar area of cortex in a cat for the same

length of time The animals were observed for 3 weeks during which they seemed normal. The frozen areas were then re-exposed. No evidence of sterile abscess or infection was found. A grayish-yellow discoloration was visible at the site of freezing, but the adjacent area was normal in appearance. On cross-section the discoloration was visible to a depth of 1 millimeter, below which the tissues seemed unchanged.

Study of the microscopic sections showed that in all specimens by far the greater part of the frozen area was entirely normal with complete preservation of cortical architecture. Damage was limited to a small portion of the frozen surface and in those areas it varied in depth between fractions of 1 and 1.5 millimeters. In some cases pathological changes were restricted to the upper layers of the cortex, whereas in others the entire cortex was destroyed. Damage did not extend below the cortex which, in these areas of the cat's brain, is between 1 and 1.5 millimeters in depth. When the damage was superficial, the injured area showed disorganization of the zonal layer with many fat granule cells. Nerve cells had partly or completely disappeared and some of those remaining were sclerosed and exhibited tortuous dendrites. Glia cells replaced damaged parenchyma. In some sections vessels were injected and occasional hemorrhage and deeper damage, the cortex was no longer visible but the white matter at these points was normal.

Microscopic examination of the area of cortex to which pressure had been applied without freezing revealed a pathological picture almost identical with that described for the frozen brain. The greater portion of the section was normal with complete preservation of cortical structure. Damage was limited to a small part which showed almost complete destruction of the cortex with replacement of nerve cells by glia. There was also some damage to the white matter beneath the cortex, where many fat granule cells were seen. At this point an attempt will be made to integrate the material that has been presented. The temperature of dry ice,  $-78^{\circ}\text{C}$ , is low enough to provide rapid freezing of

tissues without damage, as has been shown by Jahnke's work with spermatozoa and my own experiences in freezing the inferior vena cava of the cat. That brain tissue will tolerate low temperature freezing without damage has been demonstrated by the work of Koskoff and his associates with liquid nitrogen. Dry ice freezing differs from that with liquid nitrogen, in that pressure is required. The application of pressure alone without freezing has been shown to cause cortical damage almost identical with that resulting from dry ice freezing. It therefore seems likely that damage to the cortex following freezing with carbon dioxide snow is due not to refrigeration but to pressure. Application of the carbon dioxide snow-electrocautery technique to the occlusion of blood vessels of the human brain should cause little cortical damage. First of all, both freezing and coagulation are to be done on the blood vessel wall and not on the cortex. Second, if, by chance, adjacent cortex is frozen during the procedure, the injury can be but slight. For, in the experimental animal only a small part of the frozen surface was damaged, and that to a depth varying between fractions of 1 and 1.5 millimeters. In the human cortex, the greatest depth of which is 4 millimeters in the motor area, such damage should in most instances be superficial and negligible.

#### PATHOLOGY OF VESSEL THREE WEEKS AFTER FREEZING AND COAGULATION<sup>1</sup>

In order to study the long term effects of freezing and coagulating a vein, a 1 centimeter strip of the inferior vena cava of a cat was occluded. Of particular interest were the questions of permanence of closure and pathology. Three weeks after operation, the segment was found to be still occluded with many adhesions to surrounding tissues. Rupture or canalization had not occurred, and there was no evidence of sterile abscess or infection. The vessel was much shrunken and the very small lumen was completely filled with a black coagulum. Microscopic study showed that the coagulum was composed of coagulated red cells and blood pigment. The greater part

<sup>1</sup>Dr. Abner Wolf and David Cowen were of great assistance in evaluating the pathological results.

of the wall had a hyaline appearance as a result of coagulation.

#### SUMMARY

A new method for the occlusion of and the control of bleeding from large venous channels in their long axes through the combined use of carbon dioxide snow and the electrocautery has been developed. The resulting closure is permanent. The procedure is such as to do little damage to adjacent brain tissue. Application of this technique to the treatment of venous angioma of the brain has been suggested.

#### REFERENCES

- ASTAROW, V. A., and BORKOW, J. P. *Zachr. ges. exp. Med.*, 932, 80, 839-844.
- BERGMANN, E. v. *Arch. Klin. Chir.* 902, 67, 938-952.
- BROCK, S., and DYER, C. G. *Bull. New Inst.* N York, 932, 47-50.
- CHERRING, H. and BAILEY, P. *Theory and Practice of the Blood Vessels of the Brain*. Springfield: Charles C. Thomas, 1928.
- DANCY, W. E. *Arch. Surg.* 923, 7, 712-713.
- FISCHGUTH, L. v. *Zachr. ges. exp. Med.*, 1939, 77, 77-8.
- HARDY, Sir WILLIAM. *Proc. R. Soc. Lond.*, 1904, 7, 47-6.
- JACKEL, F. *Klin. Wochs.* 923, 71, 272-274.
- KOROTOFF, I. D. MARSHALL, C., and WALL, M. A. *Am. J. Surg.* 920, 50, 272-273.
- KRACER, F. *Zbl. Chir.*, 1904, 35, 61-67.
- MORAN, T. *Proc. R. Soc. Lond.* 920, 70-71.
- NILES, L. F. MARSHALL, C., and NUTLOCK, A. *Brit. J. Biol.* 94, 3, 477-484.
- REUTHER, G. *Deut. Zachr. Chir.* 877, 103, 93-95.
- PLATKE, R., ERICHSMANN, E., and REUTHER, K. *Die Konservierung von Fischen durch das Gefrieren*. Berlin: Zentral-Elektrotechnische, 1904.
- RICHARDSON, W. D. and SCHENCKEL, K. J. *Am. Chem. Soc.*, 903, 301, 5, 564.
- SPIEGELBERG, A. D. *A Basis for the Theory of Medicine*. New York: International Publishers, 1933.
- SPILLER, W. G. *Arch. Neurol. Psychiat.*, 1904, 30-38.
- WORTEN-DRUGORY, C., and BALLANCE, C. L. *Lancet*, 923, 903, 5-17.

# COMPLICATIONS AND CAUSES OF MORTALITY OF THE SURGICAL TREATMENT OF CARCINOMA OF THE COLON AND RECTUM

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SINCE July, 1937, practically all of the small and large bowel material at the Mt Sinai Hospital has been assigned to this surgical service. As a result, an unusual opportunity was afforded a group of surgeons to carry out a concentrated study of a fairly large group of patients. It is the purpose of this communication to report our experiences with which we have had to contend, the methods adopted to obviate the complications of operative fatalities. It is important to stress that many of the patients admitted to the wards of the Mt Sinai Hospital do not represent the best physical material for major surgical procedures. Serious cardiovascular disease is common, as are diabetes and kidney disease. Many of the patients have led sedentary lives with little physical exercise, with the result that muscle tone is poor and the speed of recuperation is greatly reduced. Nutritional disturbances are common, and there is great susceptibility to pulmonary infections. We are convinced that these factors are of considerable importance in influencing the mortality of major abdominal surgery in a large group of cases. There is a great difference in the physical status of ward patients living in large urban centers and those coming from rural communities. We do not believe that this has been stressed sufficiently in the past and that it may be an important reason for the disparity in the operative mortality statistics reported from various sections of the country.

We therefore formulated a plan of preoperative preparation, surgical procedure, and

postoperative care which took cognizance of the necessity of overcoming or lessening the associated disabilities with which we were often primarily confronted. The preoperative period of preparation was frequently prolonged for 2 or 3 weeks to overcome anemia, nutritional and vitamin disturbances, and to treat kidney complications and cardiovascular disabilities. Operative procedures were more often staged than not. We believe that the staging of operations for carcinoma of the colon has been the most important contribution to surgery of the colon in recent years. Finally, great care has been given to the details of postoperative care. This was found to be equal in importance to the preoperative period of rehabilitation.

Under this plan, it soon became evident that our incidence of operability rapidly increased. It seems worth while to enlarge on this aspect of the subject. Operability and mortality, of necessity, are closely related factors which influence operability have a direct bearing on mortality. A large country-wide experience has shown that, by extending the scope of operability, the mortality rate increased, but with a proportionate increase in the number of patients surviving the 5 and 10 year periods. These facts have influenced us in accepting patients for radical surgery who might otherwise have been rejected for fear of increased operative mortality. Except in rare instances and under unusual circumstances, our index of operability has not been influenced by such considerations as age of the patient, obesity, loss of weight, anemia, or associated chronic diseases. However, we are particularly wary of the patient who has had a recent coronary thrombosis. It has been our experience that these patients take radical abdominal surgery very poorly. It seems wise

to defer operation in such cases until cardiac reserve has been greatly restored. In general it may be said that our index of operability has been influenced much more by conditions associated with the growth *per se* such as situation of the tumor fixation to adjacent structures (removable or otherwise) extent of lymph node involvement, perforation and hepatic metastases. Fixation to neighboring vital structures naturally makes for inoperability but on a number of occasions it was possible to remove a section of bladder wall a loop of small intestine the entire uterus, the posterior vaginal wall or a section of the abdominal wall which had become infiltrated by an adherent neoplasm. Curiously enough, these patients have done unusually well.

The extent of lymph node involvement influences operability to a great degree and the decision to undertake radical surgery will rest, first, on the accuracy of the interpretation of the cause of the node enlargement (neoplastic or inflammatory) and second, on the experience and boldness of the surgeon. The finding of liver metastases at the time of exploration renders the situation hopeless from the standpoint of cure. However with the knowledge that patients with hepatic involvement frequently survive for 2 or 3 years, it is occasionally justifiable to resect a small movable tumor of the left colon causing obstruction or to perform an ileotransverse colostomy to short-circuit a large infected neoplasm of the right colon. We doubt that it is ever justifiable to perform an abdominoperineal resection for cancer of the rectum with associated liver metastases.

Free perforation of a colonic neoplasm still constitutes a fairly lethal complication, in spite of sulfonamide therapy. However a walled-off perforation with pericolonic abscess, most commonly encountered in the cecum and sigmoid, has not been a definite contraindication to radical surgery, provided the principles of preliminary diversion of the fecal stream and extensive drainage are adhered to.

#### PREOPERATIVE PREPARATION

It is not our purpose to describe in detail the methods utilized to rehabilitate these patients before operation. Only general principles will

be mentioned. Extending this period of preparation to 1-2 or more weeks is time very well spent. It usually pays large dividends. The diet is usually of the low residue, high caloric variety. Cleansing of the bowel is accomplished by mild purgation and colonic irrigations. With obstructing neoplasms, more and more use has been made of the Miller Abbott tube as already reported by Klem of this service. In fact, in nonobstructing tumors when a suture anastomosis is contemplated, the Miller Abbott tube is passed before operation and maintained for 5 or 6 days thereafter. However while the employment of the tube makes for a smoother convalescence, its use must be watched with care because complications due to its very presence may occur. We might mention perforation of the bowel, obstruction due to knotting of the tube and postcricoid ulceration due to prolonged use of the tube.

In acute obstruction or chronic obstruction with marked distention, ceceostomy has been performed for decompressive purposes. When complete diversion of the fecal stream is desired, transverse or sigmoid colostomy with division of the bowel is carried out. This is followed by repeated irrigations of the distal segment of bowel. Such therapy carried out over a period of 2 to 4 weeks permits restitution to normal of the previously obstructed, edematous distended, and highly infected segment of colon.

We have made practically routine use of preoperative, operative, and postoperative transfusions. Anemia is not the sole indication for transfusion. Dehydration is combated by parenteral as well as oral administration of appropriate fluids. Special care is given the urinary tract during the preoperative period, specifically in patients with cancer of the rectum. All these patients are under the careful supervision of a specially trained competent clinician who is assigned to the surgical service for this purpose. There is the closest collaboration between the surgeons and this physician at all times. We emphasize this feature as an important and desirable part of the program of the care of these patients.

Mention should be made of the routine preoperative administration of sulfanilamide

in the preparation of these patients. The senior author in collaboration with Seley reported, in 1938, the results of observations in 18 patients so prepared. These observations were controlled by careful bacteriological studies, and the opinion was expressed at that time that the incidence of postoperative peritonitis and wound infection seemed to be greatly reduced by the preoperative use of sulfanilamide. Since then, the drug has been given routinely to all patients with cancer of the large bowel. With this larger experience, we are more than ever convinced that this drug has real value in the prevention of infection. Meleney, in a recent communication, has submitted convincing evidence that the oral or parenteral administration of sulfonamides is many times more effective than its local application. However, it must not be forgotten that great importance is also attached to other details of preoperative preparation such as bowel decompression, transfusion, general rehabilitation, etc. While on the subject of sulfonamide therapy, it might be desirable to point out that the recent extensive use of the sulfonamide drugs, especially locally in the abdomen, has created among surgeons a false sense of security. While we do not wish to minimize the beneficial effects of these drugs when judiciously and carefully applied, we must emphasize that they should not be permitted to supplant careful preoperative and postoperative care and sound surgical technique. After all, the basic principles of surgery are of prime importance and must be followed, sulfanilamide or no sulfanilamide. It has been our impression that there is a tendency for many surgeons to relax their previously rigid technique because of an unwitting subconscious assurance that sulfanilamide would take care of everything. The use of sulfonamides in general surgery is practically in its infancy, and it is important that we employ these drugs with critical care so as to appraise their efficacy thoroughly. Unbounded enthusiasm is not warranted in the light of experience to date.

There has been no routine anesthesia in this group of patients. In the majority of cases, cyclopropane or ethylene with or without ether has been used. Some of the members of

the service have used spinal anesthesia. More recently, we have employed the continuous spinal anesthesia after the method of Lemon. The choice of the anesthetic agent has, in the majority of cases, been delegated to the anesthetist. An effort has been made to individualize each patient and to pick the anesthetic agent for the particular problem at hand. In the same way, we have chosen a particular operative procedure to take care of the individual problem presented by each patient. Individualization of the patient has been the prime consideration at all times.

#### POSTOPERATIVE COMPLICATIONS

The pulmonary complications have not been severe, and have influenced the mortality figures in only 3 instances. A severely toxic influenzal bronchopneumonia caused the death of a patient who had had an abdominoperineal resection. The postmortem findings were typical. The second patient also had an abdominoperineal resection and died of bronchopneumonia, which was verified at autopsy. In the third instance, a one stage ileocolic resection, the proven cause of death was bronchopneumonia. The great majority of postoperative pulmonary infections have responded quickly to sulfonamide therapy. It is apparent that these drugs have changed completely the prognosis of postoperative pulmonary complications.

The cardiovascular complications have worried us a great deal. In the entire group reported in this paper, the cause of death was proved by autopsy to be due to cardiovascular accidents in 6 instances. 5 were due to coronary thrombosis and 1 to cerebral hemorrhage. As stated before, we are particularly wary of the patient who has had a recent coronary occlusion and it would seem that the best policy is to defer surgery until cardiac reserve has been considerably improved. These patients represent a special problem which requires complete rapport between physician and surgeon. While the risk of radical surgery is greatly increased in this group, we do not believe that they should be denied the opportunity of cure of a malignant disease. We have carried out successfully extensive surgical procedures in a number of patients with severe

cardiac disease. Here the principle of individualization is particularly applicable.

The problem of wound infection after surgery of the colon has always been an important one. In the 192 operative procedures carried out in the present series, there were 22 wound infections, an incidence of 11.4 per cent. In no instance was the infection severe enough to contribute to the patient's death. We have made every effort to curtail wound infection by the following measures: (1) preoperative administration of sulfanilamide, (2) careful protection of the abdominal wall during the course of the operation, (3) rigid technique during suture anastomosis, (4) drainage through counter incisions, (5) ablating the mobilized segment of bowel when carrying out obstructive resections only after the abdominal wall has been completely repaired, and (6) the use of sulfanilamide locally in the abdominal wound. We have not been enthusiastic about the last because infections have occurred in spite of it and because it is our clinical impression that the local use of the drug delays wound repair. We believe that after the removal of large infected tumors as found in the cecum and hepatic flexure, the skin and subcutaneous tissues should be packed and left open. It must be remembered in these cases that the entire bowel wall is permeated with organisms, and in spite of rigid technique the abdominal wound becomes contaminated. It is too much to expect primary wound healing under such circumstances. For the same reason, we always institute liberal drainage of the retrocolic tissues. Perhaps this is the important reason why we have not encountered to date a retrocolic infection severe enough to impair the recovery of the patient.

The problem of wound dehiscence and evisceration has always given the surgeon considerable cause for worry. It is well known that it is particularly prone to occur in patients operated upon for abdominal cancer. About 2½ years ago after 4 instances of wound evisceration occurring in rapid succession, we changed our technique of abdominal wall suture. Since then we have used, routinely, fine alloy steel wire in the form of burned figure-of-eight sutures after the method

originally described by T. E. Jones of Cleveland. During the succeeding 2½ years in a large series of ward and private patients (over 1000) there has not been one instance of wound disruption. We have found this method of wound repair particularly applicable in the following situations: (1) after gastric resection for ulcer or carcinoma, (2) after cholecystectomy in muscular individuals, (3) after operation for colonic cancer ulcerative colitis and regional ileitis, (4) after splenectomy and (5) following hysterectomy through a subumbilical median incision. In 3 or 4 instances patients have complained of pain at the site of one of the sutures. This has been noted almost exclusively in upper right rectus incisions. In each case, the pain gradually disappeared and it was not necessary to remove the offending suture. When infection of the wound occurred, the wire sutures held the tissues together, there seemed to be less fascial slough than usual, and frequently the sutures were covered by granulation tissue without delaying wound repair or forming sinuses. Usually however in the presence of infection the sutures loosened and were removed as the infection subsided. We have been very much impressed with this method of wound closure and have no hesitancy in urging its more general use.

Bladder complications following resection of tumors of the rectum and rectosigmoid have been surprisingly infrequent. In 2 cases, the loss of vesical tone persisted for a considerable period, necessitating prolonged catheterization.

At the beginning of this study we employed the method of bladder drainage devised by Duke of St. Mark's Hospital, London. This consists of a two way irrigation system through an indwelling catheter. Experience proved however that it was better to remove the catheter 24 hours after operation and encourage the patient to void spontaneously. In most instances, the patients began to void spontaneously on the 3d or 4th day. The few bladder infections that did occur were mild and responded quickly to irrigations and sulfonamide therapy. In 1 case the membranous urethra was accidentally injured during the perineal part of the operation. With an indwelling catheter in place the opening

closed spontaneously without stricture formation.

There is one complication fortunately occurring only once in the present series, which should be discussed. In going over the literature on the subject of colonic cancer, we were struck by the fact that this complication has been rarely talked about. We refer to the post-operative retraction within the abdomen of an exteriorized loop of bowel as in the performance of an abdominoperineal resection or an obstructive resection. Experience has proved that this is a lethal complication in most instances. The surgeon must always consider the possibility of this complication and guard against it. While many theoretical reasons have been advanced for this unfortunate accident, we feel that from the practical standpoint it can be prevented by avoidance of any tension on the exteriorized segment of bowel. The bowel should project 2 or 3 inches beyond the skin surface. This requires the operative mobilization of sufficient colon to permit exteriorization in the relaxed position. Experience has also proved that a distended colon, filled with feces, the result of chronic intestinal obstruction, should rarely, if ever, be subjected to resection.

#### ANALYSIS OF CASES FOR PERIOD JULY 1, 1937, TO JULY 1, 1941

*Carcinoma of the cecum, ascending colon, and hepatic flexure.* With unobstructed neoplasms of the right colon, we have favored a two stage operation. At the first stage through a left rectus incision, operability is determined and a side to side ileotransverse colostomy or an ileosigmoidostomy is performed after division of the ileum close to the cecum. The second stage, carried out 3 or 4 weeks later through a right rectus incision, consists of an ileocolic resection to include the hepatic flexure, with drainage of the retrocolic tissues. If the first stage is performed through a left sided incision, the second stage will be much easier because of the absence of adhesions on the right side of the abdomen. We wish to emphasize this feature. Our experience with the obstructive resection operation proposed by Lahey for right sided tumors has been unsatisfactory and we have abandoned it.

TABLE 1—CANCER OF RIGHT COLON

Operation	Cases	Deaths	Percent Mortality
Two stage resection completed	7	0	0
One stage resection	6	2	33.3
Ileostomy, ileostomy, Lahey operation, etc.	17	8	47
Total	30	10	—
Operable cases	13		
Operability per cent	43.3		

During the 4 year period referred to, we have had 30 cases of cancer of the right colon (Table 1): 6 of the cecum, 16 of the ascending colon, and 8 of the hepatic flexure. Thirteen cases were found operable at the time of exploration, an operability percentage of 43.3. In the 17 remaining patients, inoperability was indicated by hepatic metastases in 12, hepatic and peritoneal metastases in 3, and peritoneal involvement in 2. In 6 instances, a one stage resection was carried out, 5 by the usual suture anastomosis and 1 by the obstructive resection of Lahey. There were 2 deaths. The cause of death in one was verified by autopsy, was bronchopneumonia and a localized abscess in the right lumbar gutter. There was insufficient drainage in this case. The second patient, a 71 year old woman on whom the Lahey operation was performed, succumbed 2 days after the colostomy was closed subsequent to a trying convalescence following the first operation. There was no postmortem examination.

In a group of 7 patients in whom the two stage operation was completed, there was no operative mortality. In another group of 14 cases, an ileotransverse colostomy or an ileosigmoidostomy with exclusion of the terminal ileum was performed. In 10 instances, inoperability precluded further surgery. There were 5 deaths in this group of 14 patients. Two, both operable, died of cardiac failure, as demonstrated at autopsy. A third patient, also with an operable lesion, died of a mechanical ileus because the wrong end of ileum was anastomosed to the colon. We wish to emphasize the care that should be exerted in visualizing the correct segment of ileum before carrying out the anastomosis. The fourth death occurred in an operable neoplasm of the hepatic flexure and, at autopsy, the cause was



TABLE II—CANCER OF TRANSVERSE COLON

Operation	Cases	Deaths	Per cent Operability
Obstructive resection	5	—	20
Ileocolostomy cecostomy	5	—	20
Total	8	—	20
Operable	5	—	62.5
Operability per cent	62.5	—	

found to be a generalized peritonitis. The suture line was intact. The fifth death occurred in an inoperable case and the post mortem examination disclosed generalized metastases. There was no indication of infection.

The 3 remaining cases of the total group of 30 died after operation. One a neoplasm of the cecum involving the ileocecal region was admitted with marked acute intestinal obstruction. Ileostomy was performed. At post mortem examination, the cause of death was found to be a generalized peritonitis due to free perforation of the tumor itself. The second patient succumbed after a Lehey operation for carcinoma of the ascending colon. Autopsy disclosed extensive lymph node metastases and a local peritonitis. We believe that this operation was a bad choice and that the surgeon should have been content with a short-circuiting procedure. The last patient was subjected to incision and drainage of an intra-abdominal abscess due to perforation of a cecal tumor. Autopsy revealed extensive liver and peritoneal metastases. There was no evidence of peritonitis.

**Transverse colon.** For operable tumors of the transverse colon we prefer the operation of obstructive resection with excision of a wide section of mesocolon. We are convinced that for the majority of surgeons, this procedure is the most radical and the safest. We do not believe that an end-to-end suture anastomosis of the transverse or left colon should be carried out unless there has been a previous complete diversion of the fecal current proximal to the site of suture. Diversion of the fecal stream cannot be obtained unless the bowel is transected as, for instance, in the Devine operation. The surgeon who routinely attempts to carry out primary resections and anastomoses will find that he is unconsciously skimping on the amount of bowel excised on

each side of the neoplasm in order to prevent tension on the suture line, and will, therefore, note a higher percentage of recurrences. We have not been impressed with the need for the Devine operation for cancers of the left colon because this procedure entails 2 major stages and 1 of a minor nature. The same can be accomplished by the 1 major stage and the minor extraperitoneal colostomy closure of the obstructive resection operation. We believe the Devine operation is particularly applicable for small tumors at or just above the rectosigmoid where an obstructive resection could not be carried out because of technical difficulties and where an abdominoperitoneal resection would, perhaps, constitute an unjustifiably radical procedure.

The results of attempts at sterilization of the contents of the large bowel in the human by the use of sulfaguanidine or succinylsulfathiazole have not been conclusive enough to warrant any undue enthusiasm or to employ operative procedures, such as primary suture anastomoses, which the surgeon would ordinarily never undertake. Perhaps the future will bring such revolutionary changes in chemotherapy that we will be able to revise completely our present methods of handling cancers of the left colon.

Of 8 cases of carcinoma of the transverse colon (Table II) 5 were found to be operable, i.e., 62.5 per cent. There was 1 death in this group of 5 obstructive resections. This patient died on the 5th day apparently of a cerebral hemorrhage. There was no autopsy. In the 3 remaining cases, ileosigmoidostomy with exclusion was carried out in 2 and cecostomy in 1. One of the patients having an ileosigmoidostomy died and the postmortem examination revealed hepatic metastases and extensive bronchopneumonia. The peritoneal cavity was clean.

**Splenic flexure descending colon and sigmoid.** There are 40 patients in this group (Table III) 25 males and 15 females. Twenty eight were found operable, an operability percentage of 70. In 27 instances, obstructive resection was carried out with 1 fatality. This patient with a descending colon tumor died on the 5th day with the clinical and radiographic signs of an acute coronary closure

TABLE III—CANCER OF LEFT COLON AND SIGMOID

Operations	Cases	Deaths	Per cent Mortality
Obstructive resection	28	1	3.5
Colostomy	8	6	75
Ileosigmoidostomy	2	0	0
Exploratory laparotomy	2	0	0
Total	40	7	
Operable	28		
Operability per cent	70		

There was no postmortem examination. The 28th case consisted of a sigmoidostomy for a malignant adenomatous polyp. The operative mortality in this group was 3.5 per cent.

In the 12 remaining cases, colostomy was performed in 8, ileosigmoidostomy in 2 and exploratory laparotomy in 2. There were 6 deaths, the essential details of which are as follows:

1. Cecostomy for intestinal obstruction was performed due to tumor of sigmoid. Convalescence was complicated by embolization of femoral artery. Death was probably due to myocardial infarction. No autopsy was performed.

2. Cecostomy was performed for perforated inoperable tumor of sigmoid. Passage of Miller-Abbott tube was unsuccessful. Death due to obvious peritonitis followed. No autopsy was done.

3. Colostomy was performed for inoperable perforated cancer of sigmoid. Autopsy revealed generalized metastases and a pelvic peritonitis.

4. This patient was a woman of 77. She had an obstructing carcinoma of the splenic flexure. Cecostomy was followed by ileosigmoidostomy. Death was due to cardiac failure. Postmortem examination revealed liver metastases.

5. Colostomy was performed for perforated tumor of sigmoid. Diffuse peritonitis was found at autopsy.

6. Colostomy for carcinoma of sigmoid with perisigmoidal abscess and perforation of bladder was done. Postoperative disruption of the wound followed. Death was due to peritonitis from spontaneous perforation of jejunum and transverse colon.

It will be noted that spontaneous perforation of a colonic neoplasm constitutes a particularly lethal complication and that, in spite of intensive sulfonamide therapy, locally and parenterally, the mortality is very high.

*Rectosigmoid and rectum.* It is not our purpose to discuss at length the various arguments for or against the many operations recommended for cancer of the rectum. Suffice it to say that, for the majority of the patients

TABLE IV—CANCER OF RECTUM AND RECTOSIGMOID

Operations	Cases	Deaths	Per cent Mortality
One stage combined abdomino-perineal resection	36	6	16.6
Two stage Lahey operation	7	0	0
Two stage Jones operation	3	1	33.3
Hartman operation	2	1	50
Lockhart-Mummery operation	1	0	0
Colostomy	2	1	50
Inoperable cases	34	11	32.3
Total	85	20	
Operable cases	51		
Operability per cent	60		

that we see, we favor the one stage abdomino-perineal resection of Miles with a permanent colostomy placed in the midline below the umbilicus. For elderly patients with low lying tumors, we employ the Lockhart-Mummery procedure of preliminary colostomy and posterior resection. If a two stage operation is indicated because of chronic obstruction, a cecostomy is performed as the first step and an abdominoperineal resection as the second. For small tumors located at, or just above, the rectosigmoid, we favor the Devine colostomy followed by anterior resection with end-to-end anastomosis. We rarely perform the two stage Lahey operation for the following reasons. The second stage has, in our hands, been a more difficult operation than the one stage abdominoperineal resection, and with preoperative sulfonamide therapy, the operation becomes unnecessary as a routine measure. If chronic obstruction is present, we believe that cecostomy is safer than the first stage of the Lahey operation.

In this group there were 85 patients who were subjected to operation (Table IV). Fifty-one were found operable, an operability of 60 per cent. In 36 cases, a one stage abdomino-perineal resection was carried out with 6 deaths, or an operative mortality of 16.6 per cent. The causes of death were as follows:

1. The patient developed extensive bronchopneumonia. The peritoneal cavity was clean. This was verified by autopsy.

2. The patient had a coronary occlusion with myocardial infarction. This was verified by autopsy.

3. Mechanical ileus was unrelieved by enterostomy. The clinical course was not that of peritonitis. No postmortem examination was performed.

4. There was wound disruption with death occurring after resuture. This case was seen before routine use of wire sutures. No preoperative sulfanilamide was given. Death was probably due to peritonitis; no autopsy was done.

5. Fulminating influenza bronchopneumonia developed; this was verified by autopsy.

6. The patient had peritonitis with paralytic ileus. A postmortem examination was performed. No preoperative sulfanilamide was given.

In the 15 remaining cases of the operable group the following operations were carried out: 7 two stage Labey operations, 3 two stage Jones operations, 2 Hartman procedures, 1 Lockhart Mummery procedure and 2 preliminary sigmoid colectomies. There were 3 deaths in this group.

1. The Hartman operation had been done. Autopsy disclosed that death was due to a spontaneous perforation of the colectomy loop with peritonitis. A pulmonary embolus was also found.

2. A sigmoid colectomy had been performed. Chronic obstruction was present on admission to the hospital. Death was caused by paralytic ileus; this was confirmed by autopsy.

3. A sigmoid colectomy had been done. Patient died of peritonitis consequent upon spontaneous perforation of a rectosigmoid neoplasm subsequent to the performance of the colectomy.

The total mortality for the operable group was 7.6 per cent.

Thirty-four patients were pronounced inoperable for the following reasons: hepatic metastases, 11 cases; inoperable neoplastic fixation to adjacent structures such as bladder, small intestine, etc., 9 cases; extreme old age or poor physical condition, 7 cases; extensive peritoneal metastases, 2 cases; metastases to tibia as proved by biopsy, 1 case; free perforation with peritonitis, 4 cases. There were 1 operative deaths. The details, given briefly, are as follows:

The first stage of a Labey operation for inoperable tumor was done. A topsy revealed extensive metastases.

Cecostomy for perforated inoperable tumor of rectosigmoid as performed. Generalized peritonitis as disclosed at topsy.

2. Cecostomy for perforated cancer of rectosigmoid was carried out. Patient was practically moribund at time of operation. The cause of death was peritonitis.

4. Colectomy was done for perforated tumor of rectosigmoid. The cause of death was peritonitis.

5. Colectomy as performed for inoperable tumor (th hepatic metastases. The postmortem examination disclosed pulmonary embolus.

6. Colectomy for inoperable growth of rectosigmoid with obstruction was performed. The topsy revealed a perforated terminal ulcer of the cecum with peritonitis.

7. Patient had perforated growth of rectosigmoid. The operation consisted of drainage of pelvic abscess, and death was probably due to peritonitis. No autopsy was performed.

8. Colectomy was carried out for cancer of the rectum with frozen pelvis. The topsy disclosed a pulmonary embolus and a small liver abscess.

9. Colectomy for inoperable tumor of rectum was done. Death was caused by pneumonia and cardiac failure as disclosed by autopsy.

10. Colectomy for inoperable tumor of the rectum was performed. No autopsy was done.

11. First stage of two stage Jones procedure was carried out. A topsy disclosed a perforation of the inverted distal loop with peritonitis, probably caused by interference of blood supply at the time of operation. The tumor was inoperable.

#### SUMMARY AND CONCLUSIONS

1. Many of the patients admitted to the wards of the Mt. Sinai Hospital present complicating medical conditions which influence, to a large extent, morbidity and mortality of major surgical procedures.

2. It is important therefore to extend the preoperative period of rehabilitation in patients with colonic cancer so as to minimize the effects of these complicating illnesses.

3. In the series of cases reported in this paper operability has been influenced more by conditions associated with the growth itself than by such general considerations as age of the patient, obesity, anemia, etc.

4. Free perforation of a carcinoma of the colon is a lethal complication in most instances.

5. The use of the Müller-Abbott tube in the preoperative and postoperative period is particularly emphasized.

6. It has been our experience that the preoperative oral administration of sulfanilamide has been a greater factor in decreasing the incidence of postoperative wound infections and peritonitis than the use of the drug locally at the time of operation.

7. Undue enthusiasm concerning the local application of sulfanilamide drugs in colonic surgery is not warranted in view of experience to date.

8. Postoperative pulmonary complications have been most beneficially influenced by the sulfanilamide drugs.

9 The cardiovascular complications constitute the major cause of postoperative morbidity and mortality in this series

10 It is our impression that wound infection has been curtailed to a great extent by the preoperative administration of sulfanilamide

11 We have, so far, eliminated the complication of wound disruption by the use of buried alloy steel wire

12 Attention is called to a rarely mentioned postoperative complication following colonic surgery, namely, retraction within the abdomen of a loop of bowel

13 For carcinomas of the right colon we favor the two stage ileocolic resection, with a 3 week or 4 week interval between the operative procedures There was no operative mortality in this group

14 We favor the operation of obstructive resection with excision of a wide section of mesentery for neoplasm of the transverse and left colon The mortality in this group was 3.5 per cent

15 We believe that a suture anastomosis of

the left colon should not be carried out unless there has been a preceding complete diversion of the fecal current

16 For small carcinomas of the rectosigmoid we favor the Devine operation consisting of a transection of the transverse colon and a resection of the tumor-bearing portion of bowel with suture anastomosis

17 For carcinoma of the rectum, our preference in most instances is the one stage Miles abdominoperineal resection

18 For low-lying neoplasms in elderly individuals we believe the Lockhart-Mummery procedure has real value

19 Finally, we wish to call attention to the fact that between 20 and 25 per cent of the patients admitted to the hospital with carcinomas of the rectum had undergone treatment for hemorrhoids during the preceding 2 to 5 months This emphasizes the importance of a carefully performed digital rectal examination followed by proctoscopic visualization in all patients who come to the physician, complaining of bleeding from the rectum

# UTERINE CONTRACTILITY DURING LABOR AND THE EFFECTS OF PARITY AND DYSTOCIA UPON IT

A Study of 105 Patients with the Lóránd Tocograph

DOUGLAS P. MURPHY, M.D., F.A.C.S., Philadelphia, Pennsylvania

THE present report deals with the uterine contractions of labor as revealed by the Lóránd tocograph (1). It is based upon observations on a series of patients who were studied at repeated intervals throughout the greater part of their periods of labor. It concerns only certain aspects of the collected data; others will be reported upon at a later date. The following relationships are considered in this communication: (1) the influence of advancing labor, (2) the effect of parity, and (3) the effect of dystocia upon the contractions. As far as can be ascertained, no similar set of observations has been published.

## MATERIALS AND METHODS

Ward patients admitted consecutively to the maternity floor of the Hospital of the University of Pennsylvania between March 22 and April 15, 1943, acted as subjects. These women received routine care which included the administration of morphine for analgesia and nitrous oxide oxygen ether for delivery.

Three trained nurses, each on 8 hour duty, secured the tocographic records of the contractions. The tocograph is a simply constructed mechanical recorder which detects uterine activity through the medium of the abdominal wall. It has been described in a previous report (2). The first tracing was made shortly after each patient was admitted; subsequent ones were secured at 1½ to 2 hour intervals. In most instances, the final tracing was made during delivery. Any unusual activity on the part of the patient or any treatment that she may have received during the recording, which might have influenced uterine activity, was noted. A fourth year medical

student recorded the clinical course of the patient's labor.

The tonus and the intermittent contractions of the uterus were studied. Each recording of uterine activity was evaluated in terms of 5 characteristics: (1) tonus, (2) wave height, (3) the sum of tonus plus wave height, (4) wave duration, and (5) wave frequency. In measuring the height, duration, and frequency of the contraction waves, the values resulted from taking the mean of 5 consecutive waves of each tracing.

The measurements are expressed in the accompanying tables in the following terms: tonus (4th column from the left) and wave height (i.e., strength of contractions, 4th column from the right) are recorded in millimeters which represent the distance traversed by the writing point of the tocograph; the duration of the contractions (3d column from the right) is expressed in seconds and their frequency (right column) is the number occurring per hour.

The sum of the uterine tonus and wave height is listed in each table, 3d column. It is assumed that this combined value represents roughly the maximum effort of the uterus.

Where differences between values in the tables are stated as being significant, they were found to be more than 3 times greater than their standard errors. Significantly high values in Tables IV to VII inclusive are designated by *italics*.

## RESULTS

*General characteristics of patients.* The study was limited to the first consecutive 105 patients admitted in labor who delivered vaginally. Thirty-four were primiparas and 71 were multiparas. Forty-nine were white and 56 were colored. Eleven individuals exhibited some degree of dystocia. The patients sup-

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TABLE I.—INFLUENCE OF ADVANCING LABOR UPON CONTRACTIONS OF 105 PATIENTS

Hours before delivery	No patients	No tracings	Mean tonus	Mean contraction wave			
				Height	Height + tonus	Duration	Frequency
18-23 9	17	38	Mm. 3 0±2 8	Mm. 4 8±2 8	Mm. 7 1±3 7	Sec. 158±88	No per hr 12 1±4 0
12-17 9	22	52	3 3±1 0	4 8±2 7	7 0±3 9	132±58	14 8±9 5
6-11 9	44	98	3 5±3 5	5 6±3 1	8 6±4 7	135±62	17 1±7 8
0-5 9	102*	264	4 5±4 0	5 9±3 2	10 0±4 5	115±51	22 1±8 4

\*Records of 3 persons unsuitable for measurement.

Table I Measurements made with a Lóránd tocograph of the uterine contractions of 105 patients, throughout the 24 hours preceding delivery. Tonus and height of contraction waves are expressed in the number of millimeters traversed by writing point of tocograph.

TABLE II.—INFLUENCE OF ADVANCING LABOR UPON CONTRACTIONS OF 34 PRIMIPARAS

Hours before delivery	No patients	No tracings	Mean tonus	Mean contraction wave			
				Height	Height + tonus	Duration	Frequency
18-23 9	11	27	Mm. 3 2±3 0	Mm. 4 0±5 2	Mm. 7 4±3 3	Sec. 154±65	No per hr 11 6±3 3
12-17 9	14	31	3 5±3 3	4 3±2 3	7 6±3 7	136±59	14 5±7 6
6-11 9	23	55	4 5±3 9	4 4±2 3	8 7±4 6	135±62	18 0±8 3
0-5 9	32*	92	5 5±4 3	5 1±2 5	10 1±4 6	109±43	23 6±7 7

\*Records of 2 persons unsuitable for measurement.

TABLE III.—INFLUENCE OF ADVANCING LABOR UPON CONTRACTIONS OF 71 MULTIPARAS

Hours before delivery	No patients	No tracings	Mean tonus	Mean contraction wave			
				Height	Height + tonus	Duration	Frequency
18-23 9	6	11	Mm. 2 4±2 4	Mm. 4 6±3 8	Mm. 6 2±4 4	Sec. 171±128	No per hr 13 3±5 1
12-17 9	8	21	2 8±2 2	5 3±2 3	8 2±4 4	126±58	15 1±7 9
6-11 9	22	43	2 2±2 5	7 1±3 8	8 5±4 9	136±60	15 9±5 1
0-5 9	69*	172	3 0±3 8	6 3±3 6	9 8±4 1	118±55	21 3±8 6

\*Records of 2 persons unsuitable for measurement.

plied 452 tocographic records made within 24 hours of delivery. Few patients supplied tracings prior to that time, such records were omitted from consideration in order to simplify the presentation. The number of tracings per patient in the 24 hour period varied from 1 to 12 with an average of 4.3.

*Influence of advancing labor upon contractions.* Table I gives the mean values of the contractions of the 105 patients arranged according to the time in labor at which their records were secured. Note (1) wide standard deviations of all measurements, (2) progres-

sive *increase* in uterine tonus and the height and frequency of the contraction waves, and (3) progressive *decrease* in duration of contraction waves. The tonus of the uterus, the strength (wave height) and frequency of the contractions *increased* progressively as labor advanced, the duration of the contractions *decreased*.

*Influence of parity upon contractions.* The contractions of the primiparas can be compared with those of the multiparas in Tables II, III, and IV. Tables II and III show the influence of the progress of labor upon the con-

TABLE IV—INFLUENCE OF PARITY UPON CONTRACTIONS THROUGHOUT THE LAST 24 HOURS OF LABOR

Parity	No. patients	No. tracings	Mean tension	Mean contractions were			
				Height	Height + tension	Duration	Frequency
Primiparas	34	205	Mm 4.2	Mm 2.1	Mm 2.4	Sec 26	No. per hr 20-24
Multiparas	7	257	274.6	232.1	232.4	27.7	24-31

TABLE V—INFLUENCE OF DYSTOCIA UPON CONTRACTIONS THROUGHOUT THE LAST 24 HOURS OF LABOR

Dystocia	No. patients	No. tracings	Mean tension	Mean contractions were			
				Height	Height + tension	Duration	Frequency
None	94	379	Mm 4.2	M 2.8	Mm 2.4	Sec 18-26.4	No. per hr 20
Present	7	257	274.6	6 cm 2.9	232.4	27.7	24-31

TABLE VI—INFLUENCE OF DYSTOCIA UPON CONTRACTIONS OF 34 PRIMIPARAS

Dystocia	No. patients	No. tracings	Mean tension	Mean contractions were			
				Height	Height + tension	Duration	Frequency
None	20	146	Mm 4.1	Mm 2.2	Mm 2.3	Sec 26.2	No. per hr 20-23
Present	14	161	252.5	4.4 2.9	4.3	26.1	17-24

TABLE VII—INFLUENCE OF DYSTOCIA UPON CONTRACTIONS OF 21 MULTIPARAS

Dystocia	No. patients	No. tracings	Mean tension	Mean contractions were			
				Height	Height + tension	Duration	Frequency
None	11	115	Mm 4.2	Mm 2.2	M 2.4	Sec 26	No. per hr 20-27
Present	10	142	274.6	232.1	232.4	27.7	24-31

tractions in the 2 groups. Table IV contrasts the measurements of both groups for labor as a whole. The primiparas experienced a significantly higher tension than did the multiparas; the latter on the other hand exhibited significantly stronger contractions than did the former.

*Influence of dystocia upon contractions.* Eleven patients experienced unusual periods of labor from the mechanical point of view: (1) 7 infants engaged occiput posteriorly of which number 2 failed to rotate to the anterior position, (2) 1 patient had an unusually large infant, (3) 2 experienced relative degrees of

pelvic contraction and (4) 1 woman had difficulty with a breech labor.

The influence of dystocia upon the contractions is recorded in Tables V, VI and VII.

Table V records the effect of dystocia upon the contractions of the 103 patients as a single group, for their last 24 hours of labor. The dystocia significantly increased the tension, the wave height plus tension and the duration of the contractions, but not the strength (height) of the contractions.

Table VI shows the influence of dystocia upon the contractions of primiparas. The dystocia significantly increased the tension, the

wave height plus tonus, and the duration of the contractions

Table VII records the influence of dystocia upon the contractions of the multiparas. In this group dystocia significantly increased the wave height (strength of contractions) but had no effect upon tonus. As in the case of the primiparas, it increased the duration of contractions. It had no significant effect upon the tonus plus wave height of multiparas.

#### EVALUATION OF STUDY

This study places on a statistical basis, for the first time, the generally accepted clinical observation of the progressive change in uterine activity which accompanies the advance of labor (Table I). It shows that change in activity can be detected early in labor, with the tocograph. It reveals one fact, perhaps not hitherto suspected, that the progress of labor *decreases* rather than increases the duration of the contractions (Table I), whereas the other characteristics increase in magnitude.

The investigation shows (Table IV) that primiparas experience a higher degree of tonus during labor than multiparas, whereas the latter exhibit contractions of greater magnitude. On the other hand, the patient's total effort, as measured by the sum of tonus and wave height, seems to be about equal both in primiparas and multiparas. The same is true of the duration and the frequency of the contractions.

Personal unpublished observations with the tocograph show that patients having rapid deliveries experience low tonus and high contraction waves. The high tonus of the primiparas, with their compensatory lower contraction waves, may be one of the chief factors

responsible for the longer periods of labor in primiparas as a group. This observation would suggest the advisability of utilizing in the delivery of primiparas those methods which are directed especially at the lowering of tonus.

The present observations indicate that dystocia increases the effort on the part of the uterus. It augments the already high tonus of the primiparas, and also the already strong contractions of the multiparas; it does not increase the tonus of the multiparas or the wave height of the primiparas. Dystocia prolongs the duration of the contractions of all patients.

#### SUMMARY AND CONCLUSIONS

1. The advance of labor brings about a progressive *increase* in uterine tonus, strength of the intermittent contractions, total amount of energy expended, and frequency of contractions. It shortens the duration of the contractions.

2. Primiparas experience a significantly higher tonus throughout labor than do multiparas.

3. Multiparas experience significantly stronger contractions throughout labor than do primiparas.

4. Dystocia significantly increases the already high tonus of primiparas and the already strong contractions of the multiparas. It prolongs the duration of the contractions of all patients.

5. The Lóránd tocograph offers a suitable means for studying the contractions of the human uterus throughout labor.

#### REFERENCES

1. LÓRÁND, S. *M Schr Geburtsh Gyn*, 1936, 103, 137-145.
2. MURPHY, D. P. *Surg Gyn Obst*, 1941, 73, 681-685.



# A STUDY OF THE POSTERIOR URETHRA IN THE NEWBORN FEMALE

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**D**URING the past 11 years there has been more research on the female urethra than at any other time. The many unexplained symptoms referable to the female lower urinary tract has prompted this research. Twinn<sup>1</sup> states that the female urethra has become only the resting place for the cystoscope in investigating the bladder. Many prominent urologists have undertaken the study of the female urethra with the idea in mind that the understanding for such symptoms would be found here.

The first investigators concluded that there were glands throughout the entire urethra, and that the group of glands found in the posterior urethra were the cause of many of these symptoms.

The purpose of this paper is to determine (a) the presence or absence of glands in the posterior urethra, (b) the nature of the folds of the urethra, (c) the structure of the urethral wall, and (d) to list and interpret other histological findings.

## HISTORY

These glands were said to be the homologue of the prostate in the male and reacted to infection in much the same manner as the prostate. For several years this remained the accepted basis for lower urinary tract symptoms in the female. Two investigators studied serial postmortem sections of the urethra in all decades of life. They found Skene's glands in the anterior third and some glandular structures and parts of Skene's glands in the middle third. At no time however were glands found in the posterior third of the urethra. Some workers felt that those structures which were mistaken for glands were in reality folds of the mucous membrane. These findings were confirmed by later investigators. Before long two different schools of thought de-

veloped as to the structure of the posterior urethra. One group were of the opinion that there were glands homologous to the prostate in the posterior third and the other believed there were none.

Folsom, in writing on the subject of the female urethra in 1931 cited a series of chronic urological cases which were referred to him. In each case the symptoms were burning, frequency and 'cold in the bladder' over a long period of time. These cases had had a thorough examination with pyelograms and kidney function tests of the upper-kidney urethra, bladder-tract the bladder and trigone had been studied carefully with the cystoscope yet, nothing could be found to account for the symptoms. The urethra was completely neglected in each instance. Folsom observed a marked inflammatory process in the posterior urethra of these females and described a "collarette" formation at the vesical neck in some. There was abundant growth of tissue in this region and it was "nicknamed" the female prostate. Because of the chronicity of symptoms and persistence of time factors in the posterior urethra of these females, particularly at the vesical neck, he believed there must be glandular elements in these tissues which would be the site of enlargement or the basis of chronic inflammation. Several photomicrographs were shown demonstrating glandular elements in the posterior urethra.

Interest in this subject was stimulated and McKenzie and Beck, in 1936 cut 50 post mortem specimens of female urethrae longitudinally in an effort to determine whether or not there were glands in the urethra and the exact nature of the mucous membrane. Nineteen cases were in the first decade of life. Five of the specimens of children were cut serially. All others were cut every 100 micra. They concluded that there were 3 types of normal bladder neck and urethra (a) smooth

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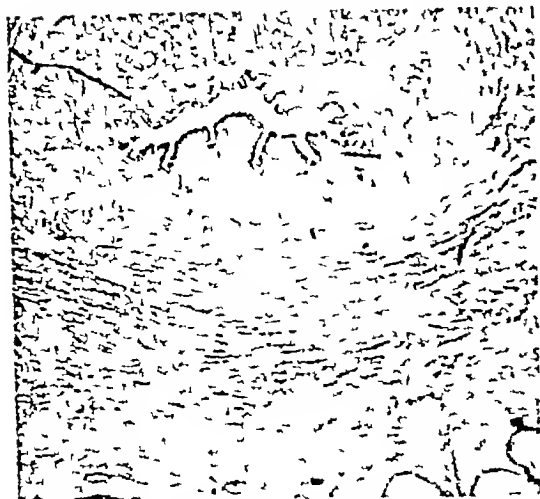


Fig 4 Cross section of urethra with all its walls intact  $\times 31$

Because of these conflicting findings by so many competent urologists it was thought that a careful study of the normal urethra, particularly in its proximal one-third where all the pathological conditions under question exist might help to throw some light on this problem. The urethra of the newborn infant would be the least apt to have been exposed to infection or trauma and, therefore, least apt to have its true anatomy and histology distorted. This may approach the microscopic picture of the normal female urethra. Reference will be made particularly as to the presence or absence of glands in the posterior urethra.

#### MATERIAL AND METHODS

Postmortem specimens were obtained from 21 fullterm infants ranging in age from 14 months to stillborn. Two additional specimens were obtained from 7 month premature infants who had lived for 24 hours. A third additional specimen was taken from a 7 month old premature infant who was stillborn. The specimens were removed from the body *in toto*, that is the entire length of the urethra with the bladder intact and part of the vagina. This was done by splitting the symphysis pubis. The body of the bladder was then removed and all retained urine was expelled. The urethra was then measured

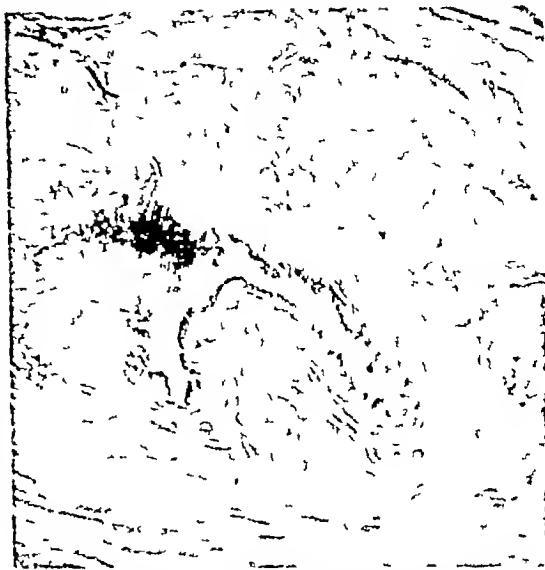


Fig 5 Cross section illustrating prominent crista urethralis. This is the large fold of muscularis mucosae forming the floor  $\times 31$

from the neck of the bladder to the meatus and from the neck of the bladder to the inter-ureteric ridge of the trigone. The trigone was then cut away from the neck of the bladder, labelled, and saved in a bottle containing 4 per cent formaldehyde. The anterior two-thirds of the urethra was then cut away from the posterior third labelled and placed in a separate bottle. A study was then made of the posterior urethra alone, and it is hoped to continue the investigations into the trigone or into the anterior urethra. All specimens were fixed in the usual manner in 4 per cent formaldehyde. Seven of the first specimens were sectioned longitudinally after the ure-



Fig 6 Cross section showing cavernous tissue under higher magnification  $\times 64$



Fig. 2. Longitudinal section of anterior half of urethra. Bulk of Skene's glands (right). Deep penetration of glands in lower mid portion. Long glandular structure seen opening into urethral lumen upper mid portion. X 60.



Fig. 3. Longitudinal section from the posterior half of the same urethra. Shows in Figure 2. No glandular structures are evident in this microscopic view. X 60.

were diagnosed as "concretion formations in the muscularis mucosae of a female urethra." In each case acinous and tubular glands were found in the posterior urethra. In one case they were also found in the trigone. Six other specimens of female urethrae were sectioned and, in each instance glands were found in the posterior urethra. He believed that the concretions originated in rudimentary

prostatic portions. No concretions were ever found in the Brunn's nests. The fact that the concretions penetrated deeply seemed to point to their prostatic origin.

Patch and Rhea, in 1935 believed that the cysts in Brunn's nests were the result of a secretory process in which tall columnar cells developed at the expense of surrounding cells and secreted mucin which was demonstrated by sections stained by mucicarmine. They believed that an irritated mucous membrane may undergo such metaplasia. These changes were followed microscopically by the author in the exstrophic bladder of a 3 year old child.

Young, in 1940, reported a case of complete urinary retention in a female 66 years of age cured by removing the obstruction with the cold cutting punch instrument. Sections of the tissue removed showed inflammation of periurethral glands and the production of marked local fibrosis. Thompson, on the other hand, reported 24 cases of vesical neck obstruction in the female which were relieved by resection. The resected specimens were studied microscopically and in no instance were glands of any kind found and he could give no reason for the cause of the obstruction. However he proposed, as a possible explanation that hyperplasia of the epithelium or hypertrophy of the sphincter muscle occurs and causes retention.



Fig. 3. Confusing fold seen in longitudinally cut section. X 4.

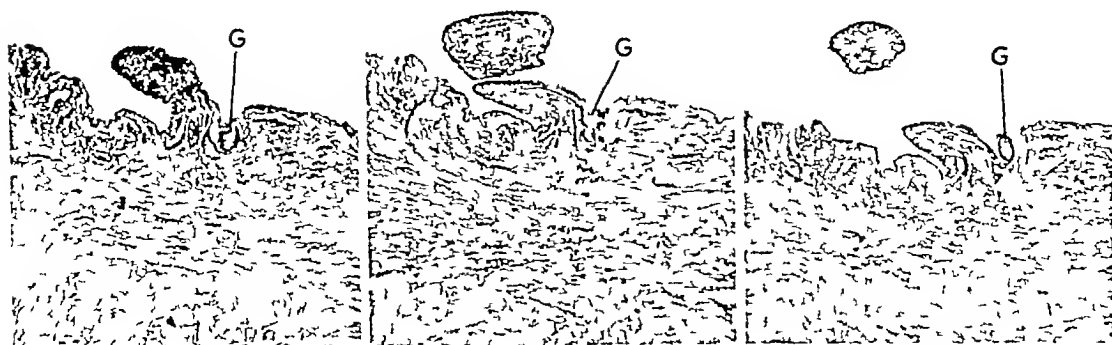


Fig 11

Fig 12

Fig 13

Fig 11 Cross section of polypoid growth taken through its base Intraepithelial gland seen at G  $\times 61$

polypoid growth leaving the floor of the urethra  $\times 61$

Fig 13 Cross section of polypoid growth nearer the bladder Intraepithelial gland still present, G  $\times 61$

### FINDINGS

In order to minimize possibilities of misinterpreting the description of findings, only the B N A terms will be used. Instead of terms such as up, down, above, and so forth, the words cephalad, caudad, proximal, and the like will be substituted.

It is agreed by all that the paraurethral, compound tubuloalveolar glands of Skene are always found occupying the anterior third and sometimes the middle third of the urethra. Its ducts empty into the floor of the urethra just proximal to the meatus. These glands have been known to encircle the urethra completely. However, in no instance

have Skene's glands ever been found extending into the posterior third of the urethra. With this in mind then, the groups of glandular structures in the posterior urethra cannot ordinarily be said to belong to Skene's glands. However, in this investigation, glandular structures found in the posterior third and found continuing distally were followed out into the middle third. The middle third was then sectioned serially to follow out the course of these structures. In other words, a distinct effort is made to study glands other than those of Skene. This study is limited as much as possible to the proximal third of the female urethra, i.e., the posterior urethra.

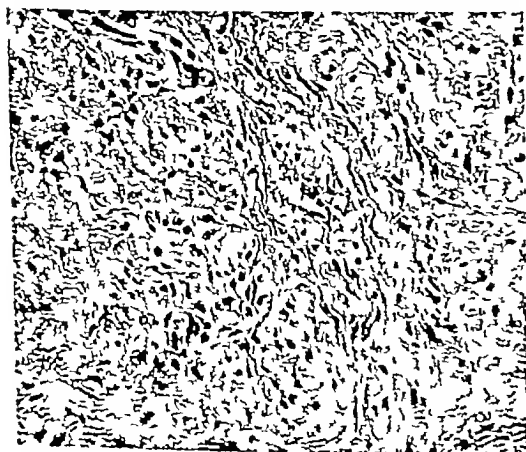


Fig 14 High magnification of growth demonstrating its connective tissue character  $\times 310$

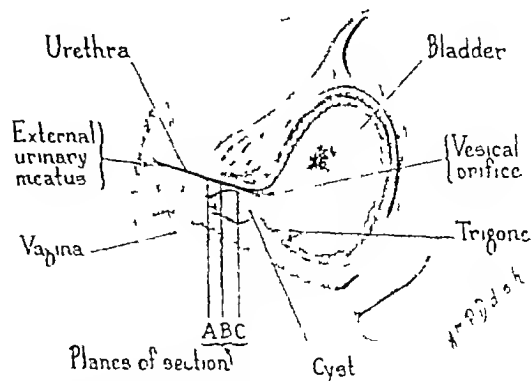


Fig 15 Schematic drawing illustrating a huge cyst of the urethral wall in the posterior third

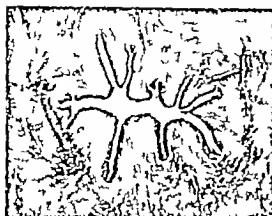


Fig. 7 Odd shaped urethra seen in cross section. Urethra all divided into 9 separate folds.  $\times 27$

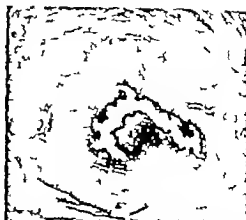


Fig. 8 Lymphocytic infiltration about the urethra. Heavily infiltrated tabs are seen hanging from the apex of all of urethra on the right.  $\times 7$

thra had been laid open by cutting through the roof. The 3 following sections were cut transversely after the urethra had been laid open and 14 were cut transversely with all sides of the urethra intact. Notes were made on all macroscopic findings. The muscular layers of the urethra as well as the superior wall of the vagina were included in each specimen for orientation.

The specimens cut longitudinally were sectioned serially every 30 to 50 micra starting in the center of the floor and moving laterally. The posterior urethrae of all cross sections were cut serially every 5 to 8 micra. Hematoxylin

and eosin was the standard stain used. However it was soon discovered that by mounting all sections on slides and by staining only every fifth slide with hematoxylin and eosin it would be possible to use special stains on parallel interesting sections as they appeared. The method proved quite successful and the methocarmine, the phosphotungstic acid hematoxylin and the Mallory stains were used. Most pathologists agree that tissue structures are usually identified by the microscopic appearance and that special stains serve only as a helpful adjunct in certain cases.

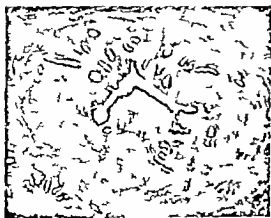


Fig. 9 Glandular structures surrounding the urethra seen in glauce. Group of glands seen lying on bed of stratified squamous in lower left hand corner.  $\times 7$

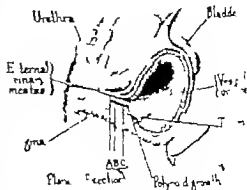


Fig. 10 Schematic drawing illustrating polyoid growth in the posterior urethra. Planes of sections described 1, B and C.

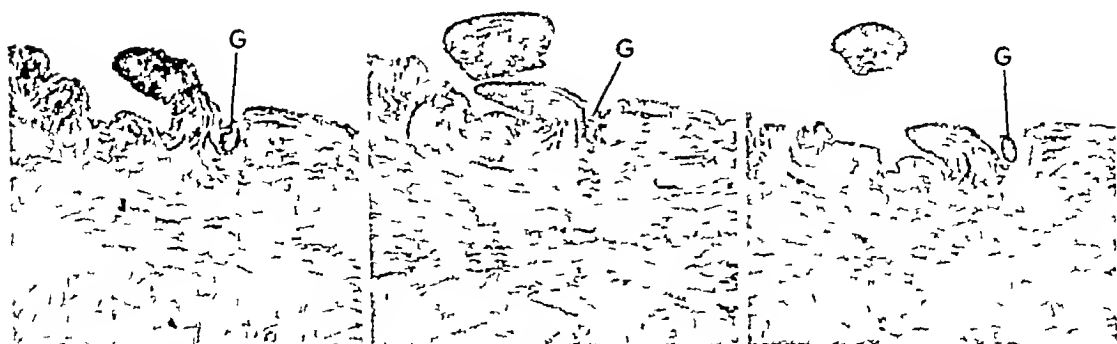


Fig 11

Fig 12

Fig 13

Fig 11 Cross section of polypoid growth taken through its base. Intraepithelial gland seen at G  $\times 61$

Fig 12 Section through B in Figure 10, showing

polypoid growth leaving the floor of the urethra  $\times 61$

Fig 13 Cross section of polypoid growth nearer the bladder. Intraepithelial gland still present, G  $\times 61$

### FINDINGS

In order to minimize possibilities of misinterpreting the description of findings, only the BNA terms will be used. Instead of terms such as up, down, above, and so forth, the words cephalad, caudad, proximal, and the like will be substituted.

It is agreed by all that the paraurethral, compound tubuloalveolar glands of Skene are always found occupying the anterior third and sometimes the middle third of the urethra. Its ducts empty into the floor of the urethra just proximal to the meatus. These glands have been known to encircle the urethra completely. However in no instance

have Skene's glands ever been found extending into the posterior third of the urethra. With this in mind then, the groups of glandular structures in the posterior urethra cannot ordinarily be said to belong to Skene's glands. However, in this investigation, glandular structures found in the posterior third and found continuing distally were followed out into the middle third. The middle third was then sectioned serially to follow out the course of these structures. In other words, a distinct effort is made to study glands other than those of Skene. This study is limited as much as possible to the proximal third of the female urethra i.e., the posterior urethra.

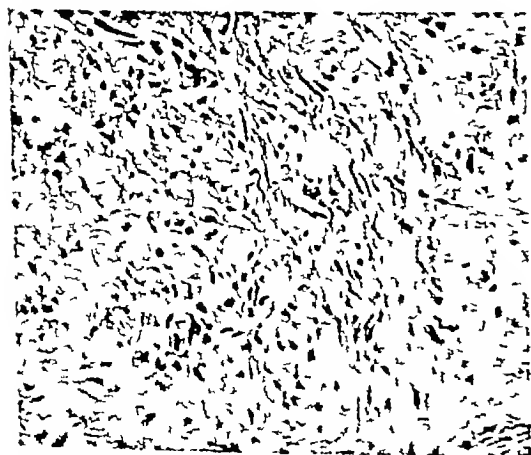


Fig 14 High magnification of growth demonstrating collective tissue character  $\times 310$

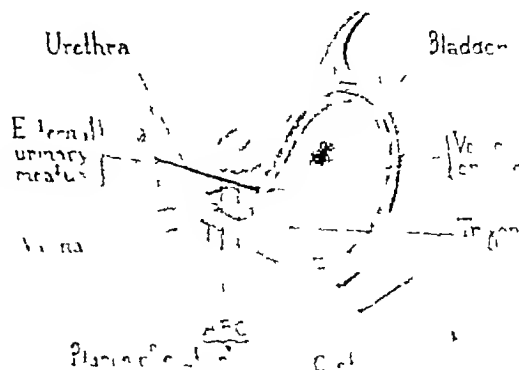


Fig 15 Schematic drawing illustrating a huge cyst of the urethral wall in the posterior third

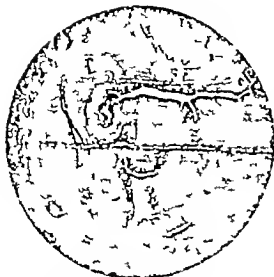


Fig. 6. Section through distal end of cyst. This is seen as small glandular structure in the lower left-hand corner  $\times 90$ .

A longitudinal section through the anterior half of a newborn urethra is shown in Figure 1. Considerable glandular tissue is seen in the upper right hand side of the photomicrograph. It will be noted that Skene's glands

penetrate practically the entire muscular coat of the urethra. These are seen in the central lower portion of the section. The terminal alveoli of these glands are made up of tall columnar epithelium. Duct structures close to the outlet of Skene's glands are lined by transitional epithelium. At the junction of the middle and anterior third a long glandular structure can be seen opening into the lumen with some mucus elements. This is demonstrated in this section and is seen emptying into the floor of the urethra at the upper center of the photomicrograph.

A longitudinal section of the posterior urethra of the same specimen is shown in Figure 2. Here we see transitional epithelium lining the urethra. The muscular coats are well described and there are no glandular structures.

It will be noted under "Material and Methods" that only the first 7 cases were cut longitudinally. A good reason for this is seen in Figure 3. A fold of the mucous membrane is seen in the lumen of the urethra in this section of the posterior urethra. This is quite confusing and such folds are entirely eliminated when cross sections are made. However, no glandular structures are seen in this photomicrograph.



Fig. 7. Photomicrograph of cross section of the cyst taken more proximally than that seen in Figure 6. Here 7 layers of squamous cells has replaced glandular epithelium  $\times 90$ .

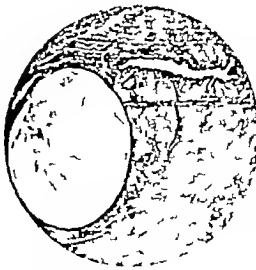


Fig. 8. Cross section of cyst taken at its widest point. Its wall has been ruptured in the upper left-hand corner of the cyst here. Lead to mucous gland or neighboring

When cross sections were made of the urethra with all its walls intact, a clear-cut well oriented picture was obtained. Such a picture is seen in Figure 4. This is the urethra of a 7 month old fetus. Folds of the urethra are clearly seen without the necessity of studying serial sections to eliminate them as glands. Small crypts are easily identified and the normal shape of the urethra is preserved. The crista urethralis is quite prominent and contains a good deal of cavernous tissue. Actually, the urethra is embedded in cavernous tissue. There are no glands seen in this specimen. The muscularis is well defined. The vaginal epithelium is clearly seen in the lowest portion of the figure and a very good picture of the thickness of the urethral floor is noted at a glance.

Another photomicrograph of a cross section of the posterior urethra of a newborn infant is seen in Figure 5. This illustrates very well the prominent crista urethralis and the cavernous tissue. Several small folds are seen projecting into the lumen of the urethra. The dark areas seen in this figure have no significance as they are merely an artifact concentration of stain. It is noted that no glandular structures exist in this posterior urethra. It may be well to add here that these are repre-

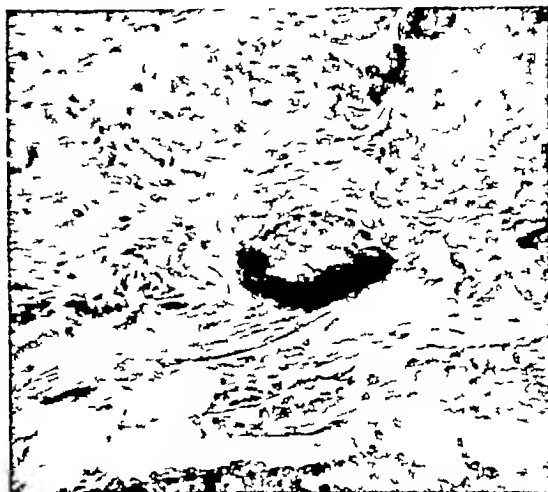


Fig 19 Photomicrograph showing a glandular structure taking the mucicarmine stain  $\times 335$

sentative photomicrographs of the posterior urethra throughout. When it is stated that no glands are seen it is meant that no glands are seen in any other part of the posterior urethra.

A high power magnification of the urethral mucosa is shown in Figure 6. This effectively demonstrates the cavernous tissue and numerous blood sinuses. In this specimen no glandular structures were seen in posterior urethra.

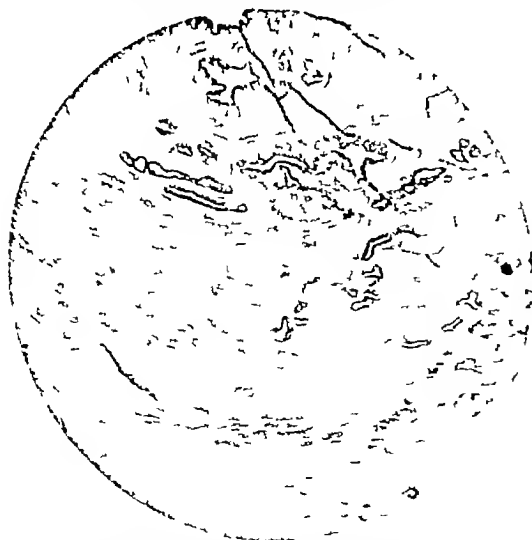


Fig 20 Cross section through posterior urethra showing lumen of urethra at top vaginal epithelium below. Upper two-thirds is studded with glandular structures  $\times 26$



Fig 21 A higher magnification of the glandular structures which are present in the section shown in Figure 20  $\times 68$





Fig. 2. Cross section of the same specimen taken at the neck of the bladder. Glands seen in mid portion on the right and in the upper left hand corner. Urethra is above and vagina is below.  $\times 25$ .



Fig. 3. Section through the prostate of newborn rat.  $\times 67$ .

The urethra never seems to retain a constant shape or assume a definite position in all specimens. It is noted in Figure 7 what an odd shape it may attain. Here there are many finger-like projections of the urethra extending in different directions dividing the urethral wall into nine folds. This is a good instance to show how longitudinal sections might easily confuse an investigator. In a cross section of an intact urethra, all out pouchings are immediately identified at a glance. There are no epithelial remnants be-

low the mucosa and there are no glandular structures seen. However there is a small nest of epithelial cells seen just to the right of the second upper vertical projection in the upper center of the photomicrograph. This is a so called von Brunn nest since it has no connection with the lining epithelium.

In 1 case a lymphocytic infiltration has been seen about the urethra. This is well demonstrated in Figure 8. The fold in the extreme right hand side of the lumen is heavily infiltrated with lymphocytes. This was in a newborn who had lived for 5 days. The crista urethralis is well outlined.

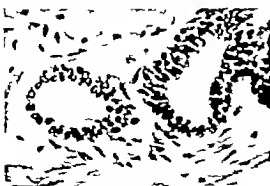


Fig. 4. High magnification of gland seen in the previous photomicrograph at the bladder neck in the female.  $\times 170$ .



Fig. 5. High magnification of glands in the prostate of newborn male. These are identical with those found in bladder neck of newborn female. Figure 4.  $\times 170$ .

The photomicrograph shown in Figure 9 from posterior urethra of Case 21 is shown here to have the reader appreciate how different this is from all others seen. It is noticed at a glance that there are many glandular structures seen about the urethra. Some of these structures in the immediate vicinity of the urethra are seen emptying into it when studied in serial sections. These structures near the urethra are lined by transitional epithelium. Some contain keratin and squamous cells but most of them do not. Here, too, at a glance the extent of these structures is seen and the muscular wall of the urethra is well outlined. There is a large group of glandular structures seen in the lower left-hand corner. These are lined by columnar epithelium with clear cytoplasm. These glands rest on a bed of striped muscle. They cannot be considered folds or epithelial nests and by studying the serial sections they are found to end blindly.

A polypoid growth was seen in the urethra in only one specimen. A schematic drawing of this growth is shown in Figure 10. This was one of the specimens in which an incision had been made through the roof in order to lay out the urethra. The growth was seen macroscopically arising from the crista urethralis. No other abnormality had been seen in this specimen. The growth occupied the entire posterior urethra and the planes of section described in this paper are shown at *A*, *B*, and *C* respectively. A cross section taken through *A* is shown in Figure 11. It demonstrates a layer of cavernous tissue in the submucosa and at the base of the polypoid growth. A small intraepithelial glandular structure is seen at *G*. No other abnormalities are seen microscopically and no other glandular structures make their appearance. A cross section through *B* (Fig 12) is taken to show where this polypoid growth leaves the mucous membrane of the urethra. A section through *C* (Fig 13) is taken closer to the bladder and here, too, there are no glandular structures. It will be noted that cavernous tissue is seen in all sections. The intraepithelial gland seen at *G* extends throughout the greater part of the posterior urethra without altering its size or position. A very high magnification of the polypoid

growth is shown in Figure 14. It consists almost wholly of the connective tissue. It might be well to add that this specimen was obtained from a 2 day old infant who died of congenital heart disease. This growth was quite prominent to the naked eye in the gross specimen and when compared to the small lumen of a newborn female urethra it assumes gigantic proportions. It is quite obvious how easily such a structure may cause an impairment of the normal urinary stream. Microscopic findings of this tissue are entirely in keeping with those of G. Thompson who studied pieces of tissue resected from the bladder necks of 24 females who had been suffering from partial urinary obstruction. As in his cases, no evidence of glandular tissue was found in the substance of the removed tissue.

The next specimen is from Case 19 in which a huge cyst was found in the lateral aspect of the floor of the urethra (Fig 15). The length of the urethra from the meatus to the bladder neck in this specimen measured 18 millimeters. The proximal 7 millimeters was embedded in paraffin and sectioned in the usual manner every 6 micra beginning at its distal end and proceeding toward the bladder. In the first 75 sections, a hyperplasia of squamous epithelium could be seen in the urethra together with several outpouchings of its epithelial lining. The mucous membrane in several instances showed intraepithelial vacuoles filled with keratin-like substance. In several places desquamated keratin was seen in the lumen of the urethra.

In the 75th section, or approximately 0.4 millimeter from the distal end of this embedded specimen, several small glandular structures appeared in the lateral part of the specimen. These were deeply embedded in the musculature of the urethra and assumed a lateral and caudal relationship to it. Each gland was lined by definite columnar epithelium with clear cytoplasm and typically flattened basal nuclei. Each individual section was carefully studied and the glands were seen to fuse as the bladder was approached. This appeared about 125 micra from its origin. The photomicrograph in Figure 16 clearly shows it with its relation to the urethra at *A*.

It may be well to note here that the urethra assumed an elongated, flattened appearance with one end turned up and the other down. There were several small outpouchings of the mucosa. As the study was carried out toward the bladder this glandular structure increased tremendously in size out of all proportion to the growth of its neighboring glands. Its lining epithelium then began to take on the character of stratified squamous epithelium with an unusually heavy layer of squamous cells. This is well seen in Figure 17.

The innermost layers of these squamous cells became detached and desquamated into the lumen of the gland. The lumen in turn rapidly became packed with desquamated cells and keratin. Glandular epithelium was no longer seen in its lining membrane. As this structure increased in size it incorporated all its neighboring glands, ruptured their walls and incorporated them into the one structure (Fig. 18). This occurred in much the same manner as a large drop of mercury incorporates its neighboring small droplets. In this way this newly formed cyst became larger and larger at the expense of its neighboring glands and it was soon packed with keratin and desquamated cells. It assumed a spheroidal shape with distended walls as if under pressure of the packed keratin in its lumen. The cyst became broadest in diameter about  $\frac{1}{4}$  millimeter from the neck of the bladder. It occupied the entire posterior urethra and, at no point, did it ever communicate with the urethra itself. In one part of the specimen it was separated from the urethra by just a few strands of connective tissue. The structure ended before the neck of the bladder was reached.

As has been stated previously only every fifth slide had been stained with hematoxylin and eosin. This being an unusual finding it was then possible to apply different stains at any given section. The mucicarmine stain was applied to several of these sections and a glandular structure is well illustrated taking the stain in Figure 19. Mucin takes a deep red stain which appears black in the ordinary black and white photomicrograph. The photomicrographs showing the relationship and size of the cyst suggest the greater pressure

exerted on the cyst from within. Fortunately this structure had not had its contents expelled spontaneously into the urethra or in the process of dissection.

What the explanation for the formation of this cyst can be is open for discussion. However there have been many recent investigations on the effect of estrogenic substances which may shed some light on this problem. One explanation offered has been that the estrogens formed in the mother pass on to the fetus through placental circulation, exert a specific action on certain epithelial structures. Squamous metaplasia of the prostatic urethra and the prostatic glands in the newborn has been well described by Brody and Goldman. Certainly there has been a change in the epithelial structure of this cyst from its definitely glandular beginning to its final keratinized stage. This may be a test application of a physiological reaction. It might be well to mention that a section taken at the broadest point of this cyst gives this structure the identical appearance of a common sebaceous cyst. There are no secretory cells and the behavior of the epithelium is like that of squamous cells of low vitality. They degenerate and desquamate into the lumen.

In the light of these recent investigations on estrogenic effects in the offspring it is pertinent to add that I have gone into the history of the mother of this infant of 4 weeks. She is a 33 year old Irish housewife who has never had a miscarriage or lues and there has been no history of endocrine disorder. Her menstrual cycle has always been regular and has been interrupted only by this first pregnancy.

A cross section of a posterior urethra of a full term infant who lived for 3 days is shown in Figure 20. Here at a glance one can see glandular structures studded throughout the upper two-thirds of the photomicrograph. The urethra is seen in the upper portion and the vagina below. Orientation here is easy and the lowermost glands are seen lying on a bed of striated muscle. The striated muscle is well brought out with the phosphotungstic acid hematoxylin stain. The glandular structures in the upper portion of the figure are lined by modified transitional epithelium.

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Serial sections show some of these communicating with one another. Only the large one just beneath the urethra communicates with the urethra and no others communicate with it or with the urethra. A high-power magnification of the structures seen lying adjacent to striated muscle is shown in Figure 21. Here the glandular nature of the structure is definite. They are lined by epithelium. A study of the sections was carried out into the bladder neck and trigone. Here, at the bladder neck, these definite glandular structures are still seen (Fig 22). They are very deeply embedded and lie almost half way between the vagina and the urethra. These structures are shown in Figure 24 at a magnification of 70. The tall columnar epithelium with clear cytoplasm is distinct. The mosaic tile appearance of the cytoplasm in one of these glandular structures at left is due to the fact that the section was cut tangentially.

The prostate of a newborn full-term male was then sectioned for comparison with the structure of the glands found in the posterior urethra of the female. Figure 23 shows glandular structures which are indistinguishable from those seen in Figure 21 under the same magnification and belonging to the female posterior urethra. At a magnification of 370 this same section of the male prostate is shown in Figure 25. In comparing this photomicrograph with that of the same magnification seen in Figure 24 it would be very difficult indeed to tell which was prostate and which was gland at the bladder neck of the female.

## SUMMARY

There has been much difference of opinion among urologists as to whether the female urethra contains glands in its proximal third. On the one hand, F P Johnson, A I Folsom, and M J Renner have found glands in a large proportion of females. On the other hand, McKenzie and Beck and Cabot and Shoemaker have studied the proximal urethra thoroughly in more than 109 routine post-mortem examinations taken in all decades of life and have found no evidence of glands in this region. Because of these widely varying opinions we decided to study the proximal

urethra in a series of newborn infants because these specimens would resemble the normal more than would specimens from later decades of life after there had been opportunity for intercurrent pathological processes. In 2 cases of 24, glands indistinguishable from those in the infantile male prostate were found. At first the study was made by cutting longitudinal sections but after we had made 7 such sections it became plain that folds and furrows also running longitudinally became confusing, and we therefore adopted the variable method of sectioning the urethra transversely with all walls of the urethra intact. In our sections the most constantly present fold in the proximal urethra was the crista urethralis. We found, also, that there was a layer of erectile tissue in the submucosa, varying widely in thickness.

Since it is not at once apparent to the general reader what could be the clinical implications of the foregoing neutral morphological facts, some such implications might well be mentioned. We have shown some additional evidence that in less than 10 per cent of cases a rudimentary female prostatic structure exists, and that the glandular elements of this structure penetrate down to the sphincter muscle, sometimes occupying the cephalic two-thirds of the urethrovaginal septum. Consequently, some females can have urinary obstruction because of hypertrophy of these glands, with or without infection. In 1 instance we found a large cyst on the floor of an infantile proximal urethra, of glandular origin with squamous metaplasia. If in later life such a cyst had ruptured into the urethra during labor or from erosion incident to infection, it would have been diagnosed as an anatomical diverticulum.

## CONCLUSIONS

This study of posterior female urethra is based on material taken from 21 full term infants and 3 seven-month premature infants. Cross sections are demonstrated as being superior to longitudinal sections in such a study. Only 2 specimens showed definite glandular tissue indistinguishable from those of the prostate in the newborn male, 21 failing to show any such structures.

2 A huge cyst of glandular origin which had undergone squamous metaplasia, probably on the basis of estrogenic stimulation was found in 1 case

3 A polypoid growth was seen in 1 instance.

4 The female urethra is embedded in carcinous tissue.

5 The crista urethralis is the most constant and prominent fold of the female urethra.

6 Glandular structures usually disappear from posterior female urethra before the 7th fetal month as shown by the fact that none of the premature specimens showed glandular structures in the posterior urethra, though only 3 such cases were studied

#### REFERENCES

1. BROOK and GOLDBLUM. Arch. Path., Chic., 940, 891 894.
2. BATHUR, A., von. Arch. path. Anat., 502, 47 74.
3. CAROT, H., and SACHSMEIER, R. T. Am. An. Ge. tounis Surgery, 936, 29. 461
4. E. ATT, E. ALYN J. J. Anat. Physiol. 1903, 65 12-30
5. FOLKOW, A. L. J. Am. M. Ass. 1911 97 341-39
6. Ideta. South. M. J. 934, 5 850
7. GIANI, R. Zbl. allg. Path. 900, 7. 20
8. HELLMUTH, GOTTSCHE. Quoted from H. D. Marx. Am. J. Path., 928, 4. 23
9. JOHNSON, F. P. J. Urol. Balt. 1920, 4 447
- JOHNSON FRANKLIN P. J. Urol. Balt., 1911, 1 3
- LOWERY O. S. Am. J. Anat. 19 2. 3 529
- LEIBEROW, O. Quoted from H. D. Marx J. Path., 928, 4. 23
3. MCKENZIE, D. W. and BECK, C. J. Urol. Balt., 1911, 36 4 4
14. PATCH, F. S. and REEL, L. J. Canad. M. Ass. J. 916 23 597
5. RIVIERE, M. J. Surg. Gyn. Obst., 911, 51. 1061
16. THORNTON, GEORGE. J. Urol. Balt., 930, 41 10
7. TOURNEUX, F. J. anat. physiol. 1859, 5 129-61
8. TWISDEN, FRANCIS P. Discussion of paper of R. E. Stevens. J. Am. M. Ass., 936, 66. 93
9. VINCOW RUDOLPH. Die krankhaften Geschwülste. Vol. 1, p. 246. Berlin: Hirschwald, 1863.
20. YOUNG, HUGH. J. Am. M. Ass. 940, 1 51 513

# THE PATHOLOGY AND TREATMENT OF INDOLENT ULCERS OF THE LEG

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**I**N spite of an improved understanding of the varicose vein syndrome, certain fundamentals have frequently been overlooked or misinterpreted. In particular, the problem of the treatment of varicose ulcers has been made difficult by lack of recognition of the underlying pathology, and by the fact that these lesions have often been confused with certain other types of ulcerations of similar appearance.

The aim of this paper is to throw light on the various elements of the problem and to indicate the channels which therapy should logically follow. Observations are presented on the common etiological factors in related types of indolent ulcers and their effect on the healing process.

## ETIOLOGY AND PATHOLOGY OF CHRONIC ULCERATIONS OF THE LEG

Indolent ulcers of the leg, whether associated with varicose veins or not, have certain characteristics in common. They are chronic necrotizing lesions which not only fail to heal spontaneously but usually become larger. They are most often situated in the lower half of the leg or around the malleoli, and appear in the center of an area of discolored and indurated skin. The edges of the lesions are rounded, fairly regular in contour and not undermined. The ulcer base is gray-yellow in color and from it is secreted a rather profuse seropurulent fluid having a characteristic disagreeable odor.

Such lesions represent the effect of a *nutritional* deficiency on the functions inherent in cutaneous cells. Defense mechanisms, reproduction, and growth, are impaired because of an ischemia arising from peripheral, arterial, or venous disturbances. This, therefore, is a disease peculiar not only to the varicose state,

but to any condition of the skin in which there is a reduced blood supply. In some cases, a decreased cardiac output may exert a further inhibiting effect.

The skin of the lower leg and ankle is particularly vulnerable to such disturbances because of the exposed location, poor protective padding over bony prominences, and a relatively meager arterial supply (Bellocq, quoted by Meisen). These factors make this region susceptible to occlusive arterial disease, trauma, or any phenomenon which may compress the subcutaneous vascular bed. Occlusive arterial lesions generally involve the whole extremity and produce a diffuse effect on the skin, while trauma or disturbances arising in veins are apt to lead to more localized changes. When more than one of these factors is present a particularly disabling lesion may develop.

Varicose indurations represent only one form of this disease. Microscopic examination of areas of this type shows atrophy of the epidermis with hyperkeratosis, loss of the rete pegs, and destruction of the hair follicles. The subcutaneous tissue is replaced by a thick layer of fibrous connective tissue containing many clumps of hemosiderin. There is a perivascular infiltration of lymphocytes and plasma cells. The blood vessels are few in number and compressed by scar tissue (Bancroft and Stanley-Brown). This fibrous scar, by choking off the circulation, inhibits cell repair, and when the skin in such an area is traumatized, bacterial invasion promptly leads to necrosis and loss of epidermis. Organisms ordinarily of low pathogenicity are able to effect this destructive process, and since healing is impeded or prevented by the nutritional state, a slowly enlarging chronic sore results.

The mass of subcutaneous scar tissue is of basic importance and is considered by many to be the result of passive congestion and

chronic edema. However Zimmerman has shown that the fibrosis is more likely inflammatory in origin and he presents the following evidence:

- 1 The long axis of the patch is usually parallel to the varix and in many instances the varicosity may be palpated as a groove or channel passing through the board like area. Infra red photography bears out this relationship.

- 2 No parallel exists between the extensiveness of the varicosities and the severity of the skin lesions. One may find extensive ulceration with small varices and conversely tremendous dilatations without evidence of skin involvement.

- 3 The area of involvement does not lie in the most dependent portions where congestion would be most severe.

- 4 The lesions are sharply circumscribed which fact would be difficult to explain on the basis of chronic congestion.

- 5 Long standing chronic passive congestion is not associated with indurations of this sort.

If one is to accept these arguments, it appears logical that phlebitic inflammatory disease forms the basis of varicose indurations and ulcers. Similarly other localized subcutaneous fibroplastic processes may lead to a circulatory deficiency of the skin, as is commonly seen following inflammatory lesions of the deep veins. How a deep phlebitis extends to involve the subcutaneous structures is still unknown. It is assumed that the process utilizes the dilated communicating veins (which are most numerous in the lower third of the leg where involvement is prone to occur) to extend outside the crural fascia. The presence of chronic capillary stasis and edema does not appear to be a primary etiological agent but probably contributes to the delayed healing of ulcers.

Local scarring may occasionally result from trauma, particularly when there is a comminuted fracture of the lower leg or ankle. Such fractures are apt to injure and thrombose the major venous trunks. In addition the vascular bed of the skin may be damaged or a large subcutaneous hematoma may form and when organized produce a dense scar mass, so

that the cutaneous circulation becomes impaired. The end result is a typical circumscribed area of discolored, brawny and atrophic skin. Ulceration is likely to follow and such ulcers progress along the same course as varicose lesions.

Once ulceration has occurred, another factor secondary infection, is introduced. Microorganisms, by stimulating defense mechanisms, further increase the amount of scar tissue present. Long standing ulcers become centered in an area of skin having an almost cartilaginous consistency and an area is involved in recurrent ulcerations tends to become more atrophic and malnourished with each attack.

Besides the factor of local scarring, other less understood elements may be involved. Obesity is a frequent complication which impedes healing. This effect may be due to hypothyroidism in some though many of these individuals have metabolic rates within normal limits.

The effect of patent and incompetent valvuloses on cutaneous nutrition is thought to be of importance only when there is marked impairment of the circulation from phlebitic scarring. The few narrowed channels which pass through the scar are able to carry only a limited amount of blood because of first the mechanical obstruction and, second the stasis and trauma produced by forces transmitted peripherally through the varices. This latter effect is ordinarily of small importance since it is spread over a wide area of capillaries, but when in combination with other circulatory deterrents, its influence is amplified.

The obliteration of varicose veins or the use of supportive bandages leads to the healing of ulcers because both forms of treatment tend to prevent distal capillary damage from pressure surges and venous stasis. These measures are therefore of value because they remove some of the load on the vascular bed and allow a more normal flow of blood. Further investigation is needed on this particular phase of the problem.

To summarize the types and factors involved in the production of indolent ulcers, the following outline is included:

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- I True varicose ulcers—the result of a phlebitis arising in superficial varicosities
- II True varicose ulceration plus some other factor
  - A Cardiac disease with decreased peripheral blood flow
  - B Occlusive arterial disease (1) Senile arteriosclerosis (2) Diabetic arteriosclerosis, (3) Funic arteritis, and (4) Thromboangiitis obliterans
  - C Occlusive or inflammatory venous disease (1) Thrombophlebitis of the deep veins, and (2) Thrombosis or obstruction of the deep venous trunks from fractures about the ankle and leg
  - D Functional venous disease—impairment of muscular activity (and of the pumping action) due to ankylosis of the knee and ankle joints
  - F Obesity—this mechanism is not clear
- III Chronic ulceration due solely to one of the factors listed under II and totally dissociated from varicosities

## THE QUANTITATIVE EFFECT ON HEALING OF FACTORS MENTIONED

It is evident that organic and functional arterial and venous lesions may profoundly influence the healing of infected cutaneous wounds of the leg. The type and magnitude of the effect may be demonstrated by applying a standard method of treatment to different cases and measuring the trend and rate of healing from week to week.

**Materials and methods** All patients were treated with weekly applications of either the Unna's paste boot or the elastic adhesive bandage because of its effectiveness, ease of application, and low cost.

Both kinds of dressing act as a supporting layer of "investing fascia" around the superficial veins and thus improve the aspirating action of muscular activity so that the veins are emptied more effectively. In addition, varicosities are prevented from becoming distended with large pools of stagnant blood. Locally, the bandage acts as a protective coat to prevent injury to delicate proliferating capillaries and epithelial cells, and by its glove-like action compresses and suppresses exuberant granulations. Douglas suggests that the elastic adhesive bandage serves a specific purpose in that it tends to draw the wound edges together, narrowing the defect.

The elastic adhesive has one disadvantage: some individuals are allergic to the adhesive mass. Of the last 100 cases treated with this

dressing, 3 developed a true allergic dermatitis. This is not to be confused with the type of rash that appears under overlapping folds of the bandage and which is due to the application of the bandage with unequal tension. Should a true sensitivity be manifested treatment is changed to the boot, which does not cause a cutaneous reaction. The boot, however, is not so efficient as the elastic adhesive and presents problems in application.

Local medications are considered of minor value. Anderson stressed the relative unimportance of local antiseptics in healing infected wounds as against general measures designed to increase tissue immunity. His experiments showed that antiseptics were generally ineffective in the presence of tissue necrosis and that delayed repair occurred when there were specific types of infection, when there were specific types of infection, when there were specific types of infection, when there were specific types of infection.

The presence of large numbers of organisms on the surface of the wound did not retard healing. All types of local application have been tried on ulcers and little or no difference was noted in the healing rate of different groups. We have, however, used certain preparations for specific effects: anesthetic ointments were used on painful ulcers, and either 2 per cent aqueous solution of gentian violet or powdered crystalline sulfathiazole was applied for their astringent and bacteriostatic action. This reduces the amount of exudate and eliminates the odor.

Records of the progress of healing were obtained by tracing the outline of the ulcers on cellophane each time the dressings were changed—over 600 such tracings were made. These were later transferred to paper record sheets, and the ulcer areas determined with the aid of a planimeter (method of Carrel and Hartman). It is realized that this is not the ideal method because it neglects the third dimension of the wound, i.e., depth. Yet when surface area is plotted against time, a curve is produced which adequately represents the trend of the particular lesion. By comparing lesions involving different factors with simple varicose ulcers, one may determine the effect exerted by these elements. In addition, calcu-

<sup>1</sup>Boots when used were applied according to a method used at the Northwestern University Clinic.



TABLE I.—HEALING RATES OF INDOLENT ULCERS TREATED WITH SUPPORTIVE BANDAGES

Type of case	Type of bandage	Number of ulcers in each group	Average (actual time in sq. cm.	Average (number of weeks until completely healed)	Average rate of healing in sq. cm. per week	Calculated rate of healing in sq. cm. per week (100% being the normal rate of rate of an
Simple varicose ulcer	Elastic adhesive	22				
		20	8.5			
	Ulcer healed		10	2	6	
Ulcers with indolent thrombophlebitis	Elastic adhesive	3			13	
				11	65	
Varicose ulcer plus the factor of obesity	Plastic adhesive			10	76	1
Varicose ulcer plus arteriosclerosis	Plastic adhesive					
			7	13	13	
			5	15	68	
5. Mixed types a. Varicose ulcer arteriosclerosis, and compensated fracture above table b. Varicose ulcer arteriosclerosis, and obesity c. Ulcers after deep phlebitis, and obesity	Plastic adhesive		6	16		
					10	
					10	54
6. Chronic ulceration associated with fracture (no varicos)	Elastic adhesive				25	6
			4		25	

lations of the rate of healing square centimeters per week for the total periods involved in repair yield an index of the effectiveness of the treatment used. A gauge is thus established which may be used to evaluate various forms of therapy. Cases selected are representative of the factors under consideration. Table I includes a summary of results.

**The simple varicose ulcer.** A total of 37 such cases was studied. 27 patients were treated with elastic adhesive bandages and 10 with Unna's boots. These ulcers varied in duration from 1 to 78 weeks, the average being 20 weeks. The associated varicosities were either 3 or 4 plus dilations and all incompetent.

The ulcers treated with elastic adhesive were all healed within 9 weeks, though one was closed as early as 3 weeks after the commencement of treatment. The curves of healing for this group of cases show a symmetrical trend not dissimilar to that observed by Douglas and Anderson.

A comparison of the healing in these 27 cases with the calculated time necessary for complete healing of defects of similar size in

normal skin is of interest (Table II). The formulas of Du Nooy were used in making the calculations. Fifteen ulcers healed less rapidly than defects in the normal skin with an average of about 2 weeks delay. Seven ulcers were healed at the same time as the theoretical lesions, and 5 healed more rapidly (about 2 weeks faster). These figures indicate that the influence of the pathological processes involved in the production of ordinary varicose ulcers is relatively small and easily overcome by the use of elastic adhesive plaster. Once the inhibitory factor is reduced to the point where cell repair is possible, proliferation proceeds at about the normal rate.

In order to establish a standard which could be used to determine the effect of various etiological elements these cases were divided into 3 groups: those ulcers smaller than 6.45 square centimeters, those between 6.45 and 13 square centimeters, and those between 13 and 24 square centimeters. This is necessary because the initial size of the lesion is important in determining the rate of healing since Carrel and Hartman and Du Nooy have shown that large wounds heal more rapidly than smaller ones. Such grouping also in-

11. ulcers are roughly graded from 10 plus, plus being the smallest and plus the smallest



which healed at a rate of 0.31 square centimeter per week.

*Ulceration induced by trauma.* Fractures of the leg and ankle may so disturb the circulation that healing of cutaneous lesions is inhibited. Two cases illustrate this.

W.D. 5 years old, had a compound both-bone fracture in the middle third of leg 20 mo. before admission. An ulcer remained at the site of the skin perforation over the crest of the tibia and was surrounded by the typical phlebotic induration which involved the lower two-thirds of the leg. Initial size of lesion was 4.2 square centimeters and the rate of healing 0.68 square centimeter per week.

H.J. 57 years old, broke his leg above the ankle 4 years prior to admission. Since this injury the ankle and foot swelled whenever he was up and around. During the last 2 years the skin over the lower half of the leg became increasingly indurated. Two years ago an ulcer appeared. When first seen this measured 2.3 square centimeters. It healed at a rate of .38 square centimeter per week.

In both these patients there was no evidence of venous dilatation.

*Several factors combined.* Where several of these conditions are involved healing is almost always very slow and irregular. Three cases illustrate this.

One patient had a varicose ulcer plus combined fracture of the ankle and advanced arteriosclerosis. Initial size of the ulcer was 4.6 square centimeters and it healed at a rate of 0.7 square centimeter per week.

There was an ulcer following deep thrombophlebitis in a very short, obese patient weighing 225 pounds. Initial size of the ulcer was 5.4 square centimeters. It healed at a rate of 0.54 square centimeter per week.

Another patient had a varicose ulcer, incompetent veins, plus obesity (20 pounds) and arteriosclerosis. Initial size of the ulcer was 4 square centimeters. It healed at a rate of .9 square centimeter per week.

*No response to supportive bandages.* In some patients when multiple inhibiting factors are present the use of supportive bandages does not result in satisfactory healing. A brief summary of 4 cases will demonstrate this.

J.Z. age 50, weighed 20 pounds. The patient had fracture and extensive deep thrombophlebitis. Thirty years before admission the middle third of the left tibia was fractured. Three years prior to admission, he developed lobar pneumonia complicated by an extensive deep thrombophlebitis of the left leg. While he was still in the hospital an ulcer appeared over the site of the old fracture. This ulcer

enlarged rapidly and on first admission was 10.1 square centimeters in area. There was a dense brawny encircling induration extending from the knee to the ankle. Elastic adhesive bandages and local applications of gentian violet were used and after 20 weeks the ulcer was reduced to 4.6 square centimeters. In spite of continued therapy there was no further improvement for the next 20 weeks. Spongio pressure was then applied, and with this the ulcer enlarged to 64.5 square centimeters. This was discontinued after 2 weeks and sulfathiazole powder applied locally under the adhesive bandage. The ulcer continued at about the same size and after a total of 84 weeks of treatment measured 55.5 square centimeters. The patient was then advised that skin grafting and a modified Koodolev operation were necessary. He refused this aid.

F.B. was 6 years old. Deep thrombophlebitis with extensive ulceration and much scarring, plus cardiovascular syphilis, were present. Fifteen years prior to admission he developed a cellulitis of the left foot. The infection led to a thrombophlebitis which was followed within a few months by the appearance of an ulcer in the middle third of the leg. He had had a 4+ Wassermann reaction for years and had received antiluetic therapy for irregular and intermittent periods. Five years ago systematic and adequate therapy was started and has been continued to the present time. When first seen the ulcer measured 37.7 square centimeters. Elastic adhesive and gentian violet were applied 2 or 3 times weekly. Sixteen weeks later the lesion was 24 square centimeters in area and continued about this size for the next 20 weeks. He dropped out of the clinic for the next 20 week period and returned with a lesion 64.1 square centimeters in size. He was again placed on the above medication and after 6 weeks has remained about the same.

A.Z. 65 years old, had a varicose ulcer with extensive local scarring and advanced arteriosclerosis. Ulcer on right leg was 4.4 square centimeters in size of 20 years duration and another on the left was 9.7 square centimeters in size of 5 years duration. One year prior to admission bilateral high and low saphenous ligations were performed without affecting the course of the lesions. Elastic adhesive was used and after 20 weeks the ulcers were larger than at the onset (right, 6.5 square centimeters; left, 11.5 square centimeters).

A.H. 67 years of age, had a varicose ulcer 3 square centimeters in size of 8 years duration. The patient was obese (20 pounds) had arteriosclerosis and extensive dense scarring from previous operations. After 56 weeks treatment the ulcer was reduced to 5 square centimeters. At this time all varices were obliterated by injections of sodium morrhuate. After more cells of elastic adhesive therapy the ulcer measured 4 square centimeters and since then has failed to become smaller.

In these cases healing was not complete after a year or more of therapy and it is ob-



induced by the fibrous deposits. More appropriate is some procedure such as complete excision of the induration with grafting or a modified Kondoleon operation which removes the dense subcutaneous scar and investing fascia. These methods make possible a new ingrowth of capillaries.

If very large ulcers are present, there is a prolonged period of disability which may be shortened by skin grafting. New skin may be applied directly to the ulcer bed (Smith) or implanted into a defect created by excision of the whole indurated area (Douglas). This latter procedure is most valuable because the scarred region is removed, allowing the ingrowth of blood vessels sufficient to maintain the vitality of the implant and prevent break down. This method is the one which is followed by us whenever possible.

#### A METHOD FOR THE EVALUATION OF OTHER MODES OF THERAPY

It is suggested that the healing rates of simple varicose ulcers, treated with elastic adhesive bandages, be used as a gauge to test the efficiency of other forms of therapy.

Such a comparison may be made in the following manner. The initial size of the test ulcer is determined with a cellophane tracing and planimeter. The area is divided by the number of weeks needed for complete healing to yield the total healing rate. This is then compared with the velocity of repair of a lesion of similar size as indicated in Figure 1 to note which treatment promotes most rapid healing.

A series of such determinations would result in a quantitative evaluation of the effectiveness of the newer therapeutic measures.

#### SUMMARY

The underlying basis of indolent ulceration of the leg is depicted as a nutritional deficiency or ischemia resulting from local circulatory changes. These fibrous deposits arise because of venous and arterial disease processes or directly from trauma to the cutaneous blood supply. The usual types of chronic ulcerations are outlined with discussion of the various elements involved.

A quantitative study of the effects of these factors is presented in order to clarify the role played by each and to indicate the effectiveness of elastic adhesive plaster in the treatment of ulcers.

Suggestions for treatment are offered and a gauge (Fig. 1) is presented, with which one may predict the healing rate of a simple varicose ulcer of any given size, or which may be used to compare forms of therapy.

#### REFERENCES

1. ALLEN, D. P. *Ann. Surg.*, 83, 64, 918.
2. BUCKHART, F. W. and STANLEY BROWN, M. *Ann. Surg.*, 90, 874.
3. CARREL, A., and HARTMAN, A. *J. Exp. Med.*, 1914, 21, 439.
4. DOUGLAS, B. *Arch. Surg.*, 1916, 22, 755.
5. DU NOY, P. L. *J. Exp. Med.*, 9, 4, 21, 451.
6. HENRI, J. *Surg. Gyn. Obst.*, 1917, 24, 298.
7. LITTLE, R. R. and KIRLEY, J. R. *Am. Heart J.*, 1926, 1, 17.
8. MERRICK, V. *Varicose Veins and Hemorrhoids*. London: Oxford University Press, 1932.
9. SMITH, F. L. *Am. J. Surg.*, 1934, 4, 67.
10. ZIMMERMAN, L. M. *Surg. Gyn. Obst.*, 1935, 61, 47.

# THE EFFECT OF VARIOUS BLOOD SUBSTITUTES IN RESUSCITATION AFTER AN OTHERWISE FATAL HEMORRHAGE

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**T**HIS study was undertaken to secure quantitative evidence concerning the value of the various blood substitutes in a hemorrhage which would be fatal if untreated. Many such substances have been tried in recent years, with conflicting reports regarding their merit. Beneficial results have been reported in which it was not shown that the experimental or clinical subjects would have died without such intervention. We have been unable to find any evidence pertaining to the therapy of traumatic shock or to the use of blood substitutes in which the recoveries observed could not be explained on the basis of chance or random sampling. The literature has been extensively reviewed recently (1, 2, 7, 15).

The reduction in blood volume is obviously the most important lethal factor in acute hemorrhage and, undoubtedly, is of major significance in traumatic shock. For its restoration many substances have been employed, including whole blood, plasma, serum, serum albumin, hemoglobin solution, red cell suspension, acacia, pectin, isinglass, methylcellulose, gelatin, and solutions of crystalloids. They have been tested by a variety of techniques which render uncertain their relative efficacy. Usually the experimental animals were subjected to general anesthesia, frequently hemorrhage was employed which was not shown to be fatal in itself, or was induced by the repeated withdrawal of small quantities of blood over a long period of time. The latter procedure affords little parallel to the clinical picture of hemorrhage as encountered in civil life or, more commonly, on the battle field, furthermore, the prolonged nature of this method involves complexities in the form of compensatory mechanisms which greatly increase the variability of the findings.

The present urgent need of a safe, adequate, and easily available medium for the replacement of lost blood volume led us to reinvestigate the problem. For this a uniform procedure was de-

vised on the basis of which the individual blood substitutes could be evaluated.

## METHOD

*Introduction.* We chose to study resuscitation from a single massive hemorrhage (a) because only one factor, namely loss of blood, is initially involved, (b) because the extent of blood loss could be measured in regard to amount and duration of the hemorrhage, (c) because a large single loss of blood is the type of fatal hemorrhage which is most likely to occur in battle or civil life, and (d) because the use of blood substitutes has not been extensively studied after massive hemorrhage.

It should be emphasized that in most of the experimental and clinical work in which blood substitutes have been used the chief therapeutic interest has been placed on the treatment of shock. Shock has been produced usually by a procedure which has resulted in hemoconcentration and not in a significant loss of erythrocytes. Shock has also been produced by removing 100 cubic centimeters of blood in an anesthetized dog and repeating the hemorrhage at intervals usually of 30 minutes until the blood pressure has reached the "shock" level. Hemorrhage of this type is not common on the battle field or in clinical practice.

*In interpreting the results obtained in this study, it is important not to confuse our results with those obtained when the blood substitutes were used to combat traumatic shock in which a severe loss of blood has not occurred.* If a severe loss of blood has occurred, then we believe that the results of our study are directly applicable.

*The method of bleeding and resuscitation.* Using healthy dogs and local procaine anesthesia, we exposed one common carotid artery and external jugular vein. A large cannula was inserted into the artery for bleeding and another into the vein for giving the transfusion after hemorrhage. Bleeding was continued until the onset of acute "air hunger" or until respiration had ceased. At this time the flow of blood from the cannula had stopped or was flowing as infrequent drops. The

TABLE I.—CONTROL HEMORRHAGE SERIES

Dogs bled the maximum amount from one carotid artery without replacement

No. of dogs	Blood loss per cent	Living	Dead	Mortality per cent
	42-70		8	80
8	39-54		8	100
14	31-59		86	
	40-44		86	
7	63-		86	
Total 39	47-70	8	42	84 (47%)

blood flowed into a graduated cylinder so its volume could be measured. The duration of the hemorrhage was recorded. It varied from 3 to 30 minutes. (It is known that bleeding from a large peripheral artery may cease after the blood pressure has been markedly reduced and time for the formation of a clot has occurred.)

When the hemorrhage had ceased, the artery was tied, and a volume of the blood substitute equal to that of the blood lost was injected into the jugular vein. The total time of the injection was about 5 minutes. The vein was tied, and the wound after treatment with sulfanilamide was closed. The animals were then observed for recovery for a period of 24 hours. Autopsies were performed in the case of death, the lungs being the chief organ inspected. Prior to death, when not immediate blood was drawn for study of pseudoagglutination. This procedure was carried out on a series of 404 dogs, including control group of 50 animals and similar groups in which the blood loss was replaced by saline serum, citrated plasma heparinized plasma, citrated whole blood, and special gelatin. Acacia and pectin were also tested. In their cases the animals were fewer in number for reasons indicated below. All solutions were injected at body temperature and were free of insoluble matter.

## RESULTS

*I. Control group.* A series of 50 animals were subjected to the procedure without replacement of the blood loss by a blood substitute.

Eighty-four per cent of the animals died after losing from 45 to 70 per cent of their total blood volume. The more detailed results are shown in Table I.

*Comment.* Since in a large group of experiments it is not feasible to determine the blood volume the blood volume of each animal was calculated on the basis of the assumption that

TABLE II.—SALINE SERIES

Blood loss replaced by equal volume of 9% NaCl

No. of dogs	Blood loss per cent	Living	Dead	Mortality per cent
	40-44			
	47-49			
8	39-54		5	62
15	53-59			
14	60-64	5		64
	65-69			
	70-			
Total 36	40-68	11	29	81

the blood volume is equal to 9.5 per cent of the dog's body weight. The dog's blood volume thus measured by various methods (4, 6, 10) has been found to range from 6 to 10 per cent of the body weight. Allowing for the specific gravity of the blood as 1.055, the blood volume was calculated as 9.5 per cent of the dog's weight in grams. In the treated groups to follow, all animals from which 40 per cent of the calculated blood volume could not be obtained were discarded.

It is to be noted in Table I that on averaging the blood loss of the different animals in groups differing by 5 per cent, the mortality was the same in each group.

*II. The normal saline series.* In a series of 9 animals the blood loss was replaced immediately with an equal volume of 0.9 per cent sodium chloride in freshly distilled water (37° C.).

The mortality was only 58 per cent after a loss of from 40 to 78 per cent of the total blood (Table II). The majority of the dogs made an immediate but temporary recovery. Consciousness was generally regained at, or slightly prior to, completion of the infusion, and the animals were alert and walking within 5 minutes. Those that died usually became comatose and dyspneic after 1 or 3 hours and expired shortly thereafter.

Thus, the saline decreased the mortality from 84 (control) to 58 per cent. This difference is decidedly significant since it is a difference that might occur by chance only in 5 out of 1000 groups of similar experiments in which 50 control and 9 treated animals were used.

*Comment.* That normal saline should be beneficial is not surprising in view of the following consideration. The animals after the massive hemorrhage still retained in their blood vessels from about one-half to one-fourth of their erythrocytes. It is known that patients with severe chronic anemia can live with 5 per cent hemo-

TABLE III —SERUM SERIES

Blood loss replaced by an equal volume of serum prepared from defibrinated blood

No of dogs	Blood loss per cent	Lived	Died	Mortality per cent
11	45-50	8	3	27
1	50-54	10	2	17
9	55-59	7	2	22
7	60-64	5	2	29
3	65-69	2	1	33
7	70-74	4	3	43
2	75-	1	0	0
Totals 50	45-76	37	13	26

globin value. So, if the erythrocytes could be kept in circulation until the circulation could compensate for an acutely decreased blood volume, then survival might be anticipated.

Holtink subjected dogs to acute hemorrhage and tested various agents, and concluded that normal saline is superior to other blood substitutes or to blood transfusion. Most opinions are diametrically opposed to this, for example, Buttle, Kekwick and Schweitzer found saline to be totally ineffective in the treatment of hemorrhage in cats. The chief reason for such discrepancies is the failure of the investigators to use a sufficient number of animals so as to avoid errors due to chance or random sampling.

The failure to reduce the mortality to a value lower than 58 per cent was due, we believed, to the possibility that the sodium chloride was not kept in the circulation for an adequate period, it "leaked out" into the tissue.

With this idea in mind we next used dog serum as a blood substitute.

**III The serum series** Fifty animals were bled as before and were given an equal volume of pooled dog's serum prepared from defibrinated blood.

The mortality was only 26 per cent after losing from 45 to 76 per cent of the total blood volume. This result is so striking that a statistical testing of the significance is unnecessary (Table III).

**Comment** It is obvious from the results that the serum was much better than the normal saline solution in resuscitating the animals. The serum, which does not leave the blood vessels, supported the circulation quite adequately by maintaining the blood volume.

**IV The use of gelatin as a blood substitute** Gelatin was first tested clinically by Hogan in 1917, but has never received a thorough trial, be-

TABLE IV —GELATIN SERIES

Blood loss replaced by an equal volume of special gelatin in normal saline, adjusted to pH 7.4 with sodium bicarbonate

No of dogs	Blood loss per cent	Lived	Died	Mortality per cent
2	40-44	1	1	50
6	45-49	4	2	33
4	50-54	2	2	50
16	55-59	9	7	44
9	60-64	7	2	22
10	65-69	4	6	60
3	70-74	3	0	0
Totals 50	40-74	30	20	40

cause other agents have been considered superior. Prejudice against gelatin has been based chiefly on its tendency to gel, its alleged antigenicity, the hazard of infection with anthrax or tetanus, and production of "intravascular clotting." Karsner and Hanzlik reported that solutions of gelatin, in common with other colloids, cause hemiagglutination.

**Pseudoagglutination due to gelatin** When a purified gelatin (5 per cent in saline solution, pH 7.4) was given to dogs after an extensive hemorrhage, death occurred. When the blood was examined it was found to be dark brown in color. On shaking the blood it became bright red, but resumed the dark color again on standing a few minutes, during which time the erythrocytes sedimented rapidly. On examination the erythrocytes were found to manifest marked pseudoagglutination. It was observed that the intravenous injection of 10 per cent dextrose solution temporarily but markedly improved the condition of the dogs which were in coma with or without "convulsions." The dextrose solution, it was found, also decreased the sedimentation and pseudoagglutination *in vitro*, but this effect was not long sustained *in vivo*, since the dextrose concentration in the blood was not maintained.

After examining *in vitro* the effect of some 12 preparations of gelatin for their effect on sedimentation rate and pseudoagglutination, one preparation of gelatin was found which has less tendency than any of the others to cause this effect. It was decided to test this gelatin on a series of animals.

**Favorable results with a special gelatin, U-17578** The gelatin was dissolved in normal saline to make a 5 per cent solution, the hydrogen-ion concentration of which was adjusted to 7.4 with sodium bicarbonate. The colloid osmotic pressure



TABLE V.—CITRATE PLASMA SERIES  
Blood loss replaced by an equal volume of plasma  
containing 5% sodium citrate as an anticoagulant

No. of dogs	Blood loss per cent	Lived	Died at once	Died in 24 hours	Mortality per cent
	40-44				100
	45-49			2	20
10	50-54				60
	55-59	1			20
8	60-64				100
	65-69				100
	70-74				100
	75-79				100
Total 30	40-79	1	1	11	70

of the 5 per cent gelatin was found to be the same as serum.

In a series of 50 animals the blood loss was replaced with an equal volume of the special gelatin solution. The mortality was 40 per cent. Thus, the gelatin solution was better but not strikingly so, than the saline since the difference observed, i.e., between 58 and 40 per cent, would occur by chance in 8 cases out of 100. However the gelatin was obviously not so good as the serum.

**Comment.** We suspect that if an ashless gelatin could be found which has no tendency to cause pseudoagglutination of erythrocytes, it could be substituted for serum in emergencies. The repeated use of such gelatin, however may not be found to be desirable though it may be found to be less foreign to the body than pectin and acacia. A gelatin solution has the objection that it gels unless held at body temperature.

The antigenicity of gelatin is now considered to be negligible, and under present methods of preparation the possibility of bacterial contamination is so exceedingly remote that it cannot be considered to be a reasonable objection.

**Inferior results with special gelatin plasma gel.** This gelatin was dissolved in normal saline to make a 5 per cent solution. It was not necessary to adjust the pH of the solution because it was 7.1 after the solution was made. A series of 10 animals were given this gelatin solution. The series was not enlarged because all 10 animals died, 6 rather promptly.

**The citrated plasma series.** Citrated plasma was used because we thought that it should prove to be better than serum. This anticipation did not prove to be true however.

The plasma used was pooled from a number of dogs. It contained sodium citrate in a concentra-

TABLE VI.—CITRATE AUTOTRANSFUSION SERIES  
Blood treated with sodium citrate to concentration of 0.35% and reinfused

No. of dogs	Blood loss per cent	Lived	Died at once	Died in 24 hrs.	Mortality per cent
	45-49			1	20
	50-54				
	55-59		1		
	60-64	1			
	65-69				
	70-74				
	75-79				
Total 10	45-79	1	1	1	30

tion of 0.35 per cent, which was the smallest concentration which would prevent the plasma from clotting.

Thirty five of the 50 animals in this series died, 23 of them immediately (Table V). Those which died at once showed respiratory failure evidenced by a long period of apnea followed by isolated gasps. A few of the animals succumbed to ventricular fibrillation during the transfusion.

**Comment.** It is apparent from these findings that sodium citrate was toxic, although the material used was chemically pure. The toxicity of this salt is well known, and the amount given clinically in the usual transfusion is innocuous. The quantity required by our animals was in excess of the safe level in the majority of cases. When 0.35 per cent sodium citrate dissolved in normal saline was given rapidly to intact (unbled) dogs in an amount equal to 60 per cent of the calculated blood volume, death resulted.

Lewisohn concluded that 2.5 grams was the fatal dose for an 11 pound dog and reasoned by analogy that 5 grams would be fatal for a 110 pound man. More recently Blairhead and others have called attention to the toxicity of sodium citrate when concentrated plasma is given. Our animals received on the average a dose of 1.0-1.15 grams for a 20 pound dog or approximately 0.11 to 0.5 grams per kilogram body weight. This is between one third and one-half the reported lethal dose for dogs which have not been previously subjected to external hemorrhage.

**Citrated autotransfused blood series.** Citrated whole blood is frequently given in relatively large quantities to human subjects, without serious reactions. However when such transfusions are given the citrated blood is generally introduced rather slowly. The rate of transfusion may account for the absence of toxicity or the presence

TABLE VII — HEPARINIZED PLASMA SERIES

Blood loss replaced by an equal volume of plasma with 20 mgm per liter of heparin as an anticoagulant

No of dogs	Blood loss per cent	Lived	Died	Mortality per cent
15	45-49	14	1	7
14	50-54	14	0	0
7	55-59	6	1	14
9	60-64	8	1	11
2	65-69	2	0	0
2	70-74	2	0	0
1	75-	1	0	0
Totals 50	45-78	47	3	6

of erythrocytes may in some way decrease the toxicity of the citrate

To determine whether citrated whole blood would be better than citrated plasma a series of 50 dogs were bled and the blood was allowed to flow into a sodium citrate solution so that the final concentration of 0.25 per cent was obtained. This citrated blood was immediately re injected into the same animal from which it was drawn. The mortality in this series was 50 per cent (Table VI), which is less than the 70 per cent mortality of the citrated plasma series, but not markedly so.

*Comment.* It would appear to be clear from these results, that when a patient has suffered a massive hemorrhage citrated plasma or citrated whole blood should be given slowly and with the idea in mind that a total dose of 15 grams for each 10 pounds of body weight may prove to be lethal. In fact, our results indicate that 0.11 to 0.15 grams of sodium citrate per kilogram may be fatal when given in plasma or whole blood after a massive hemorrhage. That is, 1500 to 2500 cubic centimeters of citrated whole blood or plasma given rather rapidly to a 70 kilogram person after a massive hemorrhage may prove to be fatally toxic.

*VII Heparinized plasma series.* It was decided to verify the toxicity of sodium citrate under the conditions of the foregoing experiments by using a different and known nontoxic anticoagulant. A series of 50 animals were given pooled plasma containing heparin (liquaemin) in a concentration of 20 milligrams per liter of blood. Only 3 of the 50 dogs died as a result of this procedure (Table VII).

*Comment.* It is apparent from the 94 per cent survival in this series of dogs that (a) plasma is an adequate replacement fluid in the case of extensive hemorrhage, (b) that return of erythrocytes is unnecessary for survival of the animal, (c) that the mortality in the preceding two series was en-

TABLE VIII — SUMMARY OF BLOOD SUBSTITUTES

No of dogs	Substitute	Lived	Died	Mortality per cent	Typical findings
50	None	8	42	84	None
50	0.07% NaCl	21	29	58	Dyspnea 2-4 hrs
50	Serum	37	13	26	None
50	Special gelatine in 0.07% NaCl pH 7.4	30	20	40	Increased sedimentation
50	Citrated plasma	15	35	70	Respiratory arrest fibrillation
50	Autotransfusion (citrate)	25	25	50	Respiratory arrest
50	Heparinized plasma	47	3	6	None
10	Pectin	0	10	100	Respiratory depression
6	Acacia I	1	5	83	Fibrillation
11	Acacia II	1	10	91	Fibrillation
17	Acacia III	5	12	71	Fibrillation
10	Plasmagel	0	10	100	Fibrillation

tirely due to the citrate, and (d) that a temporary extensive decrease in blood volume is not in itself fatal in most animals. This last point should be emphasized in considering the validity of the results of these experiments.

*Miscellaneous blood substitutes.* Three acacia solutions from different manufacturers and one pectin preparation were tested. The mortalities were 5 out of 6, 10 out of 11, and 12 out of 17 for the three acacias. When pectin was tested on 10 dogs, all the animals died rather promptly. The findings for all substances tested are listed in Table VIII. These substances all cause pseudoagglutination, which is sufficient to be fatal after an extensive hemorrhage.

# DISCUSSION

We believe that the method devised by us for the evaluation of blood substitutes is an adequate one for their evaluation. It is drastic to the extent that if a solution is ineffective, or is in itself toxic, these effects will be manifested in the form of a high mortality. On the other hand, the animals will survive if a nontoxic and efficacious medium is given.

The prompt but temporary recovery of most animals on saline injections indicate that this procedure has value in case of emergency, with the obvious necessity of further treatment with a more potent preparation with the least possible delay. In this latter category may be placed heparinized plasma or serum. Regarding gelatin, the material we have used is definitely superior

to citrated plasma and to the other artificial blood substitutes tested, but it falls far short of perfection. Further refinement of the product is required in this connection. It is encouraging that the mortality has been brought down from 100 per cent on the first products tested to a final magnitude of 40 per cent.

The high toxicity of citrate when given in the amounts required as an anticoagulant for the large volume of plasma required under our experimental conditions is, we believe, a contraindication for the use of citrated plasma when hemorrhage is extensive. The reason for the great superiority of heparinized plasma over serum is at present obscure. It is obviously not due to the presence of fibrinogen in the one and its absence in the other but more likely to certain alterations in the protein content which occur during the preparation. Varying degrees of serum toxicity have been reported (3, 14). Acacia and pectin, as now available, are totally unsuitable as blood substitutes when the hemorrhage is extensive.

#### SUMMARY AND CONCLUSIONS

After a massive hemorrhage, such as occurs after the section of a large peripheral artery the intravenous infusion of normal saline solution will save some lives. The hemorrhage used in these experiments had a mortality of 84 per cent. This was reduced to 58 per cent when saline was given after the hemorrhage.

1. Pooled serum proved to be better than normal saline, the mortality from the hemorrhage being reduced from 84 to 26 per cent.

3. When citrated plasma or citrated whole blood was used, the amount of citrate that had to be given in replacing the blood lost was toxic. Hence caution must be exercised in giving citrated plasma and citrated whole blood in quantities of more than 1200 cubic centimeters to patients who have lost from 40 to 50 per cent of their blood. This is especially true when the citrated whole blood or plasma is given rapidly.

4. Heparinized plasma was found to be the safest and most effective blood substitute tested, since the mortality from the hemorrhage was reduced from 84 to 6 per cent. Heparinized plasma is an adequate replacement fluid in the case of ex-

tensive hemorrhage: the return of erythrocytes unnecessary for survival of the animal.

5. All the gelatins we have studied, with the exception of two cause marked pseudocoagulation of erythrocytes. A gelatin which caused at least pseudocoagulation *in vitro* reduced the mortality from the hemorrhage from 84 to 40 per cent.

It is believed that if a gelatin can be found which will cause no pseudocoagulation, it will prove to be a good blood substitute for emergency use. Plasma gel was not found to be suitable.

6. The gum acacia and pectin solutions we have used to date cause pseudocoagulation and have a lethal effect when used as a blood substitute after a massive hemorrhage. That is, after two-thirds of the red blood cells have been lost, the pseudocoagulation of the remainder by gelatin, acacia, or pectin may be fatal.

7. It is believed (a) that the citrated human plasma now available for use should be accompanied by the precaution that it be injected slowly and not in unlimited quantities in patients who have suffered a massive hemorrhage and (b) that the label should carry a statement regarding the toxicity of sodium citrate.

#### REFERENCES

- AMERSON, W. E. *Biol. Rev.* 1937, 12, 43.
- BLALOCK, A. and MASON, M. F. *Ann. Surg.* 1937, 105, 657.
- BOND, D. D. and WRIGHT, D. G. *Ann. Surg.* 1941, 113, 500.
- BROOKS, P., ROBERT, C., and SMITH, G. F. *J. Physiol. Path. Gen.* 1939, 12, 2.
- BUTLER, G. A. A., KIRKWOOD, A., and SCHWARTZ, A. *Lancet*, Lond. 1940, 340.
- CHAMBERLAIN, N. and QUINLAN, E. J. *J. med. physiol.* 1932, 2, 204.
- HARRIS, H. V. *Surgery*, 1941, 3, 417.
- HODAN, J. J. *J. Am. M. Ass.* 1939, 11, 104.
- HODAN, A. W. *J. Ill. Surg. Gyn. Obst.* 1938, 31, 143.
- HOOPER, C. W., SMITH, H. P., BILLY, A. E., and WATKINS, C. H. *Am. J. Physiol.* 1939, 5, 107.
- KARLBERG, H. J. and HANSEN, P. *J. Physiol. (Lond.)* 1939, 4, 479.
- LEWIS, R. *Proc. Gyn. Obst.* 1941, 37.
- MITCHAM, E. E., AMERSON, C. T. and HILL, J. M. *Surgery*, 1941, 14.
- STICHMEL, M. M., WATKINS, J. A., and MORROW, J. *J. F. Ann. Surg.* 1940, 6.
- WRIGHT, C. J. *Physiol. Rev.* 1941, 21.

# SLIDING OR PARAPERITONEAL HERNIA OF THE PELVIC COLON

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**S**LIDING hernia may be defined as an extrusion of an organ in such a way that the visceral peritoneum forms part of the sac. In other words, it protrudes alongside the sac, that is, paraperitoneally (Fig. 1). It may appear to be within the sac, but it is not completely surrounded by it.

The term sliding hernia<sup>1</sup> has never seemed appropriate to many of us because these hernial masses cannot slide back into the abdomen without carrying the sac, in part at least, with them. The contents of an ordinary hernia may slide readily because of the slippery covering of two layers of peritoneum, both completely surrounding the extruded viscus: the visceral layer or serosa, and the hernial sac which in ordinary hernias corresponds to parietal peritoneum. In a paraperitoneal or sliding hernia, the viscus is incompletely covered by the same two layers and there is an area which is devoid of peritoneum altogether.

It is said that a sliding hernia may be suspected before operation by palpation, by the broadness of the internal ring and by the ineffectiveness of a truss. However, the diagnosis of

<sup>1</sup>English: Sliding slip; slipped; gliding; extrasaccular; parasaccular; paraperitoneal. German: Gleitbruch. French: Hernie par glissement. Italian: Ernia per sdrucciolarmente. Latin: Hernia labens.

the sliding or paraperitoneal nature of the hernia is usually made only at operation. It, therefore, behooves all who treat hernia patients to know how to manage this type safely. Recognition of the condition and understanding of its true pathological anatomy are of great importance, not only for the cure of the hernia but also for avoidance of surgical errors which may endanger the life of the patient.

"The sac in such cases is not complete, being deficient at the posterior and outer part of the gut, where natural cellular connexions exist. Strangulation is less liable to occur. 'It is,' says Scarpa, 'by carrying the incision too much along the outer side of the hernial tumour that the operator fails to open the sac in this variety of hernia when he has arrived at the cellular covering of the intestine, would not scruple to divide it, and thus would only be made aware of his mistake by the discharge of the faecal contents.'" (3)

Moschowitz in 1925 emphasized the mistakes in the diagnosis and treatment of sliding hernias, and described the rational surgical management. Graham in 1935 gave a clear and concise account of the condition with diagrams which depicted the abnormality and its correction. Unfortunately, the facts set forth by these authors have not had the widespread acceptance they deserve.

The distinction between a paraperitoneal or sliding hernia and an ordinary hernia with adhe-

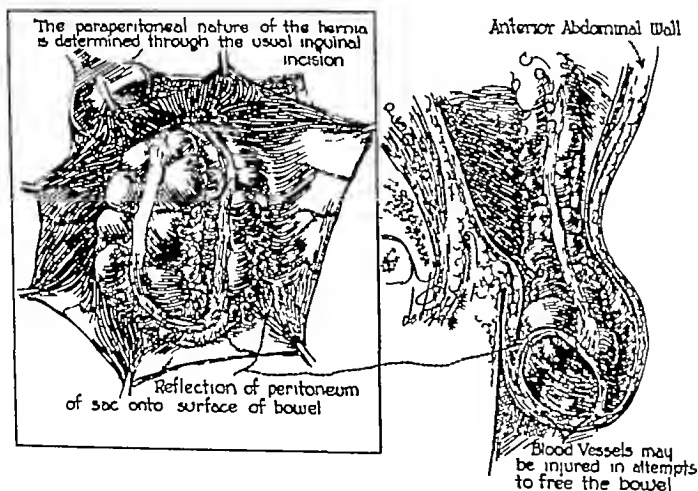


Fig. 1

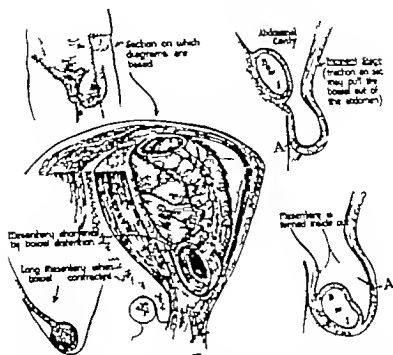


Fig. 2.

sions to the sac should be clearly understood. Adhesions may be safely cut preparatory to reduction, excision of the sac, and repair. But in a patient with sliding hernia, attempts to free the bowel may injure its blood supply.

Even when the diagnosis is understood there are dangers to the bowel and its blood supply inherent in certain unanatomical methods of repair which have been described and which are apparently in common use. It is difficult to close the deep inguinal ring properly and safely unless the bowel is not only reduced but also kept away from the groin. Some operations designed to reconstruct the mesentery and invert the sac by successive pursestring sutures may kink the bowel or leave raw areas within the abdominal cavity and tend to fasten the bowel to the groin where it is endangered by the placement of stitches for closure of the large internal ring and the inguinal canal.

The urinary bladder may enter the inguinal canal along with a peritoneal sac as a true sliding or paraperitoneal hernia. This condition is easy to understand because the bladder is normally an extraperitoneal organ. The relationship of the peritoneal folds may be somewhat confusing when there is a paraperitoneal hernia of an organ such as the pelvic colon that is normally completely

surrounded by peritoneum, both visceral and parietal. This may also happen to the terminal ileum when it descends as a sliding or paraperitoneal hernia with the cecum. The leaves of the mesentery unfold and turn inside out to form the hernial sac (Fig. 2).

In a fixed cadaver the layers of the sigmoid mesentery are very definitely demarcated, but in life the mesentery is a variable fold. The peritoneum is not very stretchable when the bowel distends the leaves of the mesentery separate to become serosa of the bowel (Fig. 2). The parietal peritoneum is especially movable over the underlying tissues in the lower parts of the abdominal cavity and the pelvis. The position shifts in accordance with visceral demands. This mobility is familiar to us in peritonizing raw surfaces after the excision of various organs. When one remembers these physiological changes in the position of the peritoneum it is not difficult to understand how the sigmoid mesentery may be unfolded in such a manner as to place the colon in the retroperitoneal or paraperitoneal position of a sliding hernia.

#### METHOD OF REPAIR

Small sliding hernias may be safely and adequately repaired by simple reconstruction of the

# BROWN SLIDING HERNIA OF THE PELVIC COLON

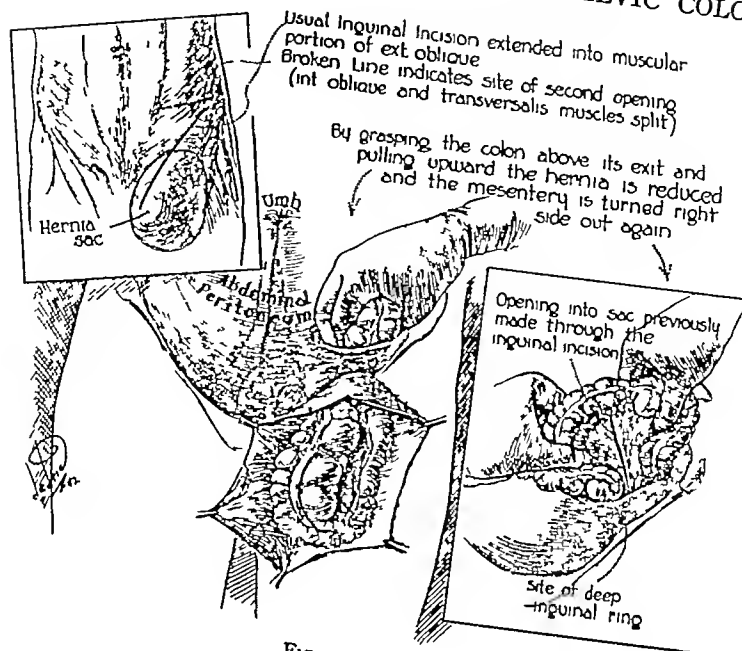


Fig 3

groin through the usual incision. But many dangers are eliminated when a separate incision into the peritoneal cavity is used to reduce the hernia and repair the peritoneum while it is held away from the groin. A low rectus incision may be used (1, 9). It is simpler to retract the upper part of the herniotomy wound, strip the external oblique aponeurosis upward, and enter the peritoneal cavity by separating the fibers of the internal oblique and transversalis muscles in the direction of their fibers (Fig 3). This technique is essentially the same as has been described by Torek for appendectomy in combination with herniorrhaphy. LaRoque (4, 5, 6) emphasized the advantages of such an approach for operations on inguinal hernias.

We believe that the muscle splitting incision should be made some distance from the deep inguinal ring to avoid leaving a narrow band of muscle devoid of nerve supply.

Through this upper incision the bowel is grasped above its entrance into the groin and reduced by traction. This maneuver pulls the bowel out of the groin and brings with it the peritoneum which formed the sac. It is interesting to note that when the bowel is brought up the opening which has been previously made at or near the fundus of the hernia sac may now be found at the mesenteric border of the colon (Fig 3). The sac is made up largely of the lateral leaf of the

mesentery of the iliac colon, which has been turned inside out.

After reduction, the opening in the sac is closed with a running suture which is carried along to fold together any redundancy of peritoneum that is present. It may be considered a wise step to anchor some stitches through to the medial leaf of the mesentery at an avascular point near its root.

The structures of the inguinal canal are then reconstructed by whatever method seems wise. Suture of the transversalis fascia may be carried out completely because the bowel and its vessels have been removed from the site of operation. The upper incision is not closed until after the deep layers of the inguinal canal have been repaired so as to allow palpation and inspection of the repair of the groin from within the peritoneal cavity.

## SUMMARY

Sliding or paraperitoneal hernias of the pelvic colon present certain difficulties and dangers when repair at the inguinal canal is attempted. A separate opening into the peritoneal cavity enables one to demonstrate that in such cases the sac is largely composed of the mesentery of the colon turned inside out. Traction on the bowel above its entrance into the hernia restores the normal anatomy of the peritoneum by turning the

everted mesenteric right side out again. Appropriate repair of the inguinal canal is made simple and safe when the bowel is carried away from the groin.

## REFERENCES

- GRAM, R. R. *Ann. Surg.*, 935, 92, 784.
1. HORSLEY J. SKELTON, and BIGGER, L. *et al.* *Operative Surgery* Vol. 2, pp. 848-849. St. Louis C. V. Mosby 940.
2. KEY, C. *Annals*. Editorial footnote, vol. 6, pp. 65-66. Cooper, Sir Ashley. *Anatomy and Surgery Treatment of Abdominal Hernia* London and Philadelphia, 844.
3. LAROCHE, G. P. *Surg. Gyn. Obst.*, 1940, 77, 27.
4. *Idem.* *Ann. Surg.*, 924, 79, 375.
5. *Idem.* *Arch. Surg.*, 932, 24, 189.
6. MACCARTHY, L. S. *Canad. M. Ass. J.*, 1936, 34, 174-77.
7. MOORE, F. F. *Surg. Gyn. Obst.*, 912, 1, 112.
8. MORGENTHAU, A. V. *Ann. Surg.*, 925, 2, 112.
9. SCARPA, A. *A treatise on hernia*, Edinburgh, 1814.
10. TOLLE, FRANK. *Ann. Surg.*, 1900, 43, 665-67.

# ENTERIC INTUSSUSCEPTION IN ADULTS

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**T**O introduce this paper, two statements are quite essential as a working basis. First, acute enteric intussusception in the adult is an entity that is encountered only occasionally during the lifetime of the average surgeon. Second, polyps in the colon are quite common, and their occurrence in the small intestine is rather rare, but a combination of polyps in both the large and small bowel is almost unique.

This statement serves to clarify the purpose of this paper. The case to be reported is one of an acute jejunal intussusception which occurred in an adult in whom we later discovered multiple polyps of both the large and small intestine. Such a case seems to warrant reporting.

## CASE REPORT

E E, a 25 year old white male, complaining of pain in the abdomen and across the lumbar region, was admitted to the Station Hospital, Fort George G Meade, Maryland, on January 10, 1941.

The essential history dated back to 1935, at which time he suffered an attack of pain in the rectum associated with bleeding, a constant desire to defecate, and a mass which protruded from the anus. He was taken to a hospital and a polyp with a long pedicle was snared off. Following this experience, the patient was quite well for the next 4 years. In 1939 he suffered another episode almost identical to his first attack, and a polyp was found and removed. Again there was a period of partial well being until the onset of his present illness which took place on December 21, 1940. However, the patient did recall having had a persistent backache and marked constipation during the past year.

On December 21, 1940, while on duty at Camp Livingston, Louisiana, about one hour prior to going on Christmas leave, the patient developed sudden severe pain in the lower left abdomen. He was able, however, to start a trip to his home in Wisconsin. The pain gradually subsided but was followed by a feeling of nausea which returned several times during his stay at home, and on a few occasions he actually vomited. He returned to his camp in Louisiana on January 2, 1941, still not feeling well, but he did not seek medical attention.

On January 6, 1941, he was ordered from Camp Livingston to Camp Holabird, Maryland, arriving there late the night of January 8, 1941. During the entire trip the patient ate very little and was disturbed by nausea, vomiting, abdominal cramps and backache, but constipation was no worse than usual. The following day he developed a frequency of urination, having to void about every half hour, and the pain in his back had become more severe. On January 10, 1941, he was transferred to the Station Hospital, Fort George G Meade, Maryland, with a tentative diagnosis of perirenal abscess.

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The patient was seen by one of us (W H G) on admission and found to be markedly dehydrated. There was excruciating tenderness over both kidneys. The abdomen was mildly distended with no rigidity and no local tenderness, but rather a vague diffuse discomfort on deep pressure. There had been no bowel movement for over 48 hours so an enema was given. The fecal material obtained showed no evidence of the presence of blood. Rectal examination was negative, as was a spot film of the abdomen. Urine revealed 4 plus albumin, specific gravity 1.035, with clumps of leucocytes, many granular casts, bacteria, and yeast cells seen on microscopic examination. Blood pressure was 124/80, pulse, 86, temperature, 100.6 degrees Fahrenheit. Complete blood picture was normal except for leucocytosis of 15,300.

The entire picture was most confusing and it was felt that the original impression of perirenal abscess was probably the most likely. The patient was given a large amount of intravenous fluids and tolerated a moderate intake of water by mouth without vomiting. He was observed frequently during the next 12 hours with little or no change in condition. However, about 5:00 a.m. on January 11, 1941, after having been able to rest rather well without sedation, the patient experienced extreme pain in the abdomen and vomited some dark brown fluid which contained blood. The abdomen was somewhat more distended and had a "doughy" feel to it. The pain had entirely left the renal region and centered around the umbilicus. Peristalsis was audible. Impression of acute intestinal obstruction was made and the patient prepared for operation.

Operation was performed by Dr W H Gerwig, Jr, January 11, 1941. Under pontocaine spinal anesthesia, the abdomen was opened through a long right paramedian incision. A hard mass which could be delivered was located lying in the pelvis. This was found to be a gangrenous, irreducible intussusception involving about 2½ feet of the jejunum. A resection of the mass was carried out and an end-to-end anastomosis was performed. Hurried examination of the adjacent bowel revealed no palpable polyps. The abdomen was closed in layers without drainage. The specimen removed was then opened, and no organic etiological lesion such as a polyp could be found (Fig 1).

During the next few days, the patient had a rather stormy course but began to improve gradually and was allowed up after 17 days.

One morning about 4 weeks following operation (February 16, 1941) the patient was having a stool and a small mass passed the anus but was attached higher up by a long narrow pedicle. The pedicle was ligated and cut, with great relief to the patient. He then admitted that at each stool for the past week he felt a dragging down type of pain in the lower left abdomen.

The patient was allowed several weeks convalescence after which a careful survey was begun. Repeated proctoscopic examinations were negative, and no information was obtained from 2 barium enemas (Fig 2). Urine findings no longer showed any indication of renal damage.

It was not until a double contrast barium enema x-ray visualization was carried out that any positive information could be gained. The colon was first filled with barium which was then expelled, after which the colon was inflated



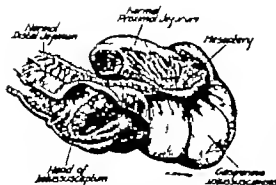


Fig. Specimen removed but not opened.

with air and x-ray pictures were taken. These films clearly showed flecks of barium that had adhered to and definitely outlined several large polyps located in the region of the splenic flexure and sigmoid (Fig. 3).

On May 9, 1941 the patient was discharged on certificate of disability after arrangements had been made for him to be sent to the Church Home and Infirmary Hospital, Baltimore, Maryland. He was admitted to that institution on May 17, 1941, and preparations for operation were begun.

Operation was performed by Dr. Harvey B. Stone, May 26, 1941. Under general anesthesia the abdomen was opened through left paramedian incision. The site of the original intussusception was found to be about 3 feet distal to the ligament of Treitz and was well healed and patent. A polyp, about the size of normal adult ovary was located some 4 inches proximal to the original intussusception. The jejunum, as opened, the pedicle ligated, cut, and the polyp removed. The jejunum was then closed. No other polyps could be felt in the small intestine. The large intestine was then explored and 5 polyps could be felt in the region of the splenic flexure and resection of this area was carried out meticulously over Stone clamps. The abdomen was then closed in layers without drainage. The patient had satisfactory course and was discharged June 9, 1941. Since that time the patient has written to us at monthly intervals and states that he has been symptom free and in excellent health.

When the section of colon removed at operation was opened, not only were the 5 palpable polyps found, but numerous others too small to be felt were seen on the mucosal surface (Fig. 4). Microscopic sections of the colon and jejunal polyps revealed characteristic type of adenomatous neoplasia. This completed the proof that ours was case of multiple adenomatous polyp involving the small and large intestine, one of which had probably caused the acute jejunal intussusception.

It is difficult to explain the confusing symptomatology indicative of kidney disease which the patient manifested when first seen. This is especially true since the urine cleared up so rapidly. We believe that the disturbance of fluid balance caused by dehydration was too great a burden for his borderline renal capacity and that he developed a renal azotemia with urinary changes. When the fluid balance was readjusted, kidney function returned to normal.

#### DEFINITION, CLASSIFICATION, HISTORY AND ETIOLOGY

Intussusception is a term used to designate a condition in which there is invagination of a part of the intestines into an adjacent part. The portion that is invaginated is called the "intussusceptum," and the portion that receives the indigitation is known as the "intussusceps."

From an anatomical standpoint, 4 distinct varieties are recognized: (1) enteric, (2) ileocolic, (3) ileocolic, and (4) colic.

These terms merely designate the site at which the intussusception occurs. The enteric and colic types may occasionally be multiple. At times we sometimes see multiple intussusceptions which are of no clinical significance, but are merely a result of changes that take place in the bowel at the time of the patient's death.

On the basis of etiology there are 2 types, the primary and the secondary. The primary or acute type is not uncommon and occurs chiefly in infants at the ileocolic region. There is usually sudden onset. An underlying lesion is seldom found in these cases, and when once reduced for do not usually recur. The secondary or chronic recurrent type usually occurs in adults or older children and an organic causative factor is frequently present which, if not removed, will tend to cause recurrence. Various conditions have been reported as the cause of the secondary type of intussusception and will be discussed more fully later in this paper.

The mechanics of intussusception when an organic lesion is present are more than a simple traction of the lesion. Panton reported a case of enteric intussusception in which the tumor was proximal to the invagination. In our own case a tumor was found when the affected area was resected and it was only at the second operation that an adenomatous polyp was discovered a number of inches proximal to the previous intussusception. By drawings and illustrations of several specimens, Ward<sup>11</sup> showed that the lesion which actually causes a secondary intussusception is proximal to the invagination, in the intussusceptum, or at the apex. Therefore, he is of the opinion that the process is one of more than mere mechanical traction, and is actually assisted by spasm of the bowel at or near the site of the offending lesion. When the spasm occurs, there is relaxation of the intestine just distal to the spasm so that the contracted portion may be retracted. We believe that this is probably a satisfactory conclusion. However he goes further and attempts to put the primary intussusception of infancy on the same footing as the secondary b-



Fig 2, left Roentgenogram after barium enema, negative



Fig 3 Roentgenogram showing flecks of barium adherent to and outlining polyps in region of splenic flexure

tussusception of adults, and states that in these babies there is a definite inflammation of lymphoid tissue in the terminal ileum. When this condition is present, spasm of the bowel at this site takes place, with relaxation of the ileocecal valve and cecum. The contracted or spastic ileum is then drawn into the relaxed cecum by the longitudinal muscle fibers. However, until more substantial proof is available, this process must remain purely hypothetical. Ladd and Gross reported 372 cases of intussusception in children, 87 per cent of whom were under the age of 2 years. In 354 of these cases, pathogenesis of the intussusception could not be found.

Regardless of the cause, intussusception of the small intestine is extremely rare. McClure relates only 7 such cases in 350,000 patients admitted to the Henry Ford Hospital. Large bowel intussusceptions in adults are more frequent. MacDermott reported 5 cases of this type that occurred in his practice in less than 1 year. Webb and Sheinfeld reviewed 4 cases that they observed in a rather short period of time.

As has been previously mentioned, there are many lesions reported as the cause of the adult or secondary type. Benign and malignant neoplasms, Meckel's diverticulum, gumma, ulcers of dysentery, typhoid fever and tuberculosis, enterocysts and parasites such as round worms have all been mentioned in the literature.

It is generally agreed that neoplasms are by far the most frequent cause of secondary intussusception. However, many of these tumors may never

give rise to the condition. In the large bowel the chief offender is a malignant tumor while in the small intestine benign neoplasms, especially the adenomatous polyps and lipomas, are most often encountered as etiological factors. In 1917 King was able to collect from the literature only 47 cases of benign tumors of the small gut. In 1931 Raiford reviewed the records of the Johns Hopkins Hospital and found 34 primary benign neoplasms of the small bowel, about 60 per cent of which were adenomas. Rankin and Newell in 1933 reviewed 35 cases of true primary benign tumors of the small intestine, which represented the total number at the Mayo Clinic. At that time, theirs was the largest series of its kind. They found that the benign growths occurred less frequently than

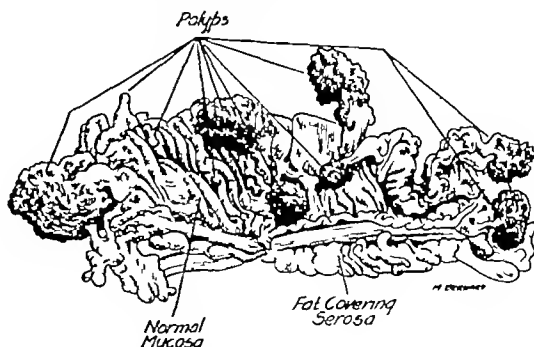


Fig 4 When section of colon was opened numerous small polyps on mucosal surface were disclosed in addition to the 5 polyps which were palpable

the malignant variety but of the benign tumors, the adenomas made up the greater number of cases. Fluke also found that adenomas occur more than any other benign tumors of the small intestine but are only rarely present in the jejunum. Botzford and Newton, Cooper and other men feel that lipomas are the most common benign tumors of the small intestine. Poston in 1935 was able to collect only 64 cases from the literature. During the same year Kirschbaum found 12 benign tumors of the small bowel in 5,754 consecutive autopsies, 6 of which were lipomas. Comfort, Aspinall, Wilmoth, and others have collected small series of cases and believe lipomas occur more frequently.

Our opinion in the matter is that because only a small percentage of these benign neoplasms of the small intestines give rise to clinical symptoms, a true evaluation is almost impossible.

Any tumor of the intestines is a potential cause of intussusception, and unless there is a definite contraindication it should be removed. This is especially true if the growth is an adenomatous polyp, for these polyps tend to undergo malignant changes. Lawrence has reported 532 autopsy findings of polyps of the gastrointestinal tract, with malignant transformation in from 6 to 7 per cent. It is in the descending colon, sigmoid and rectum that polyps bear the closest relationship to malignancy. This relationship is least in the small intestine and transverse colon.

In every case of a adult intussusception, a careful search should be made to try to discover causative lesion as it is frequently present, not only as evidenced by our own case but also by reports of Oughterson and Cheever, Gussane, and Faber who all describe recurring intussusceptions requiring multiple operations for relief. However it is not difficult to understand how easily these tumors may be overlooked when the surgeon is dealing with a distended, shocked, ill patient whose bowel is obstructed. One is naturally inclined to omit a careful search of all the intestines at such a time, and instead do as little as possible. In many cases this conservative attitude is commendable; however, it must be remembered that the cause may still be there and every reasonable effort should be made to determine what the cause is. Later when the patient's condition permits, x-ray studies or possibly a secondary exploration may be advisable.

In the opening words of this paper we stated that the occurrence of adenomatous polyps in both the large and small intestine is almost unique. Reference is made to the 532 autopsy reports of Lawrence dealing with polyps of the gastroin-

testinal tract. In only 4 cases of the entire series did polyps exist in both the large and small bowel.

#### SYMPTOMATOLOGY

The symptomatology of infantile and adult intussusception is not the same. The intussusception encountered in young babies has a rather characteristic clinical picture. In a young healthy infant who suddenly begins to have colic-like pains, passes blood from the rectum, develops an abdominal mass, and shows signs of intestinal obstruction such as vomiting, distention and constipation, a diagnosis of acute intussusception is inevitable. On the other hand, the adult who develops an intussusception may present a variety of signs and symptoms dependent on the size and severity of the lesion. A preoperative diagnosis of intestinal obstruction is usually made and the causative intussusception found at operation. If the intussusception is in the small bowel, symptoms of high obstruction are present, and if in the colon, the picture is that of a lower obstruction. Bleeding from the rectum is recognized only occasionally and a mass may or may not be felt. Because of the tendency to chronicity of the adult type of intussusception, a history of frequent attacks of colic-like pains without obvious etiology makes recurring intussusception a possibility to be considered.

#### TREATMENT

The proper treatment of either the infantile or adult type is surgical intervention unless the former is promptly reduced by an enema. In the latter a careful search for the cause must be made. Osborne operated upon a patient with intussusception of the jejunum who gave a history of severe intermittent abdominal pain for 3 years. Simple reduction was carried out at the first operation. Four weeks later the abdomen was again opened to search for the cause. A lipoma was found and two strictures were also present which were separated by healthy bowel. He produced the intussusception and found that one stricture fell at the site of the apex and the other at the junction of the encircling and retreating area. This is mentioned to show that these areas are the most vulnerable parts of an intussusception.

When possible reduction is the best procedure in infantile intussusception. These little patients do not tolerate large operations very well, and when the intussusception is once reduced there is seldom a recurrence. In the adult type either reduction or resection may be carried out. The latter is often necessary and may be followed by a primary anastomosis, or by establishing an in-

testinal stoma This may be done by any of the well known methods, such as the Mikulicz-Paul method, the Rankin method, or other similar procedures

Tumors, when found, should be removed When these are single or if there are only a few in different regions, they can be removed separately through simple openings in the bowel If several are localized in a section of bowel, this segment should be removed In case there is widespread distribution as seen in diffuse polyposis of the colon, especially when there is bleeding or beginning obstruction, a one or two stage colectomy following a primary iliosigmoidostomy would seem warranted, with fulguration of any polyps present in the rectosigmoidal stump Polyposis of the entire colon with definite malignant changes may demand preliminary ileostomy and then total colectomy and removal of the rectum, followed by deep therapy The 2 last mentioned procedures are extensive, mutilating operations, but they seem justifiable when we consider that polyps, especially in the lower large bowel, are precancerous lesions

#### SUMMARY

A rather unusual case of adult jejunal intussusception is presented Further studies revealed that the patient also had the almost unique condition of polyposis involving both the large and small intestine Emphasis is placed on the importance of a double contrast barium enema x-ray visualization of the colon when performing gastrointestinal studies The definition, classification, mechanism, and etiology of intussusception are discussed Intestinal tumors are considered, especially those of the small bowel with reference to

frequency and possible malignant changes, particularly in the adenomatous polyps The symptomatology and treatment of intussusception are brought out with special emphasis on the necessity for location and removal of the organic etiological agent which is so frequently present in the adult type of intussusception

#### REFERENCES

- 1 ASPINALL, ARCHIE *Med J Australia*, 1936, 1 820
- 2 BOTSFORD, T W, and NEWTON, F C *Surgery*, 1941, 10 265
- 3 CLUBBE, C P B *The Diagnosis and Treatment of Intussusception* 2d ed London Oxford University Press, 1921
- 4 COMFORT, M W *Surg Gyn Obst*, 1931, 52 101
- 5 COOPER, H G N *Brit M J*, 1939, 1 328
- 6 FABER, J E *Proc Mayo Clin*, 1936, 11 299
- 7 FISKE, FREDRICK A *Ann Surg*, 1927, 106 221
- 8 GISSANE, WILLIAM *Brit. J Surg*, 1937-38, 25 608
- 9 KING, E L *Surg Gyn Obst*, 1917, 25 54
- 10 KIRSCHBAUM, J D *Ann Surg*, 1935, 101 734
- 11 LADD, WILLIAM E, and GROSS, ROBERT E *Arch Surg*, 1934, 29 365
- 12 LAWRENCE, JOSEPH C *Am J Surg*, 1936, 31 499
- 13 MACDERMOTT, E N *Brit. M J*, 1935, 1 1214
- 14 MALLORY, TRACY B *N England J M*, 1936, 215 883
- 15 MCCLURE, ROY D *Detroit, Mich. Personal communication*
- 16 MCGLANNAN, ALEXIUS *South M J*, 1916, 9 977
- 17 MCGLANNAN, ALEXIUS, and McCLEARY, STANDISH *J Am M Ass*, 1927, 89 850
- 18 OUGHTERSON, ASHLEY W, and CHEEVER, DAVID *Surg Gyn Obst.*, 1929, 48 682
- 19 POSTON, R. I *Brit. J Surg*, 1934-35, 22 108
- 20 RAIFORD, THEODORE S *Radiology*, 1931, 16 253
- 21 RANKIN, FRED W, and NEWELL, CECIL E *Surg Gyn Obst*, 1933, 57 501
- 22 WARDILL, W E M *Brit J Surg*, 1925-26, 13 158
- 23 WEBB, GEORGE, and SHEINFELD, WILLIAM *Am J Surg*, 1928, 41 315
- 24 WILMOTH, CLIFFORD LEE *Am J Surg*, 1936, 31 567

# FULL THICKNESS DEFECTS OF THE CHEEK INVOLVING THE ANGLE OF THE MOUTH

## A Method of Repair

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THE repair of full thickness defects of the cheek is complicated by the necessity of providing a substitute for the mucous membrane and by the fact that part of the work must be carried out in an infected field. The experiences of DeGraefe, Roux, Dieffenbach and other pioneer workers in this branch of surgery are recounted by D'Ammon and Baumgarten in their book on plastic surgery published in 1843. In most instances repair was undertaken with no antecedent experience or precept, but the results were often very good.

Gussenbauer (9-10) in 1877 appears to have been one of the first to undertake restoration of the cheek, including mucous membrane, with a definite plan in mind. The problem was presented by a boy 7 years old whose jaws were held together by scar tissue resulting from a gangrenous stomatitis. Gussenbauer raised a quadrilateral flap the pedicle of which was placed in front of the ear and the free end at the angle of the mouth. He then cut through the entire thickness of the cheek from the mouth to the masseter muscle and brought the free end of the flap around the edge of the masseter to the inside of the mouth and sutured it to the mucous membrane. At a second operation 4 weeks later the pedicle was cut through and the whole flap with the skin surface inward was sutured in the defect. A similar second cheek flap was later put on the raw surface of the first to provide an external covering of skin.

The idea of replacing mucous membrane by skin, apparently initiated by Gussenbauer has been utilized in a number of procedures. Israel, in 1887, described a method of repair in which he used a flap from the neck; the pedicle was placed just behind the angle of the jaw and the distal free end was turned into the cheek defect so that the skin surface replaced the missing mucous membrane. At a second operation the pedicle was cut across near its origin and the portion of flap not already utilized was folded over on the external raw surface of the distal end to provide an external skin covering. Hahn, in the same

year, described a method very similar to that of Israel except that he employed a flap from the chest with a broad pedicle placed at the clavic. Gersuny, also reporting in 1887, replaced the mucous membrane of the cheek by raising a flap from the upper neck. The pedicle was placed along the mandible and the flap was nourished by the subcutaneous tissue only. Von Hacker, 1883, raised a flap from the neck to serve as a substitute for mucous membrane and used a second flap to cover the external raw surface. Kraske, 1883, closed full thickness defects by raising a flap from the immediate vicinity of the opening and turning it into the defect. The outer raw surface was covered with a Thiersch graft. The pedicle of the flap consisted of subcutaneous tissue without the overlying skin.

Ceerny in 1880, introduced a modification of Israel's procedure by turning under the distal end of a long flap and allowing time for the opposing raw surfaces to become firmly fused before transplanting the graft. At the time of transplantation the end of the flap had a covering of skin on both surfaces. Bardenheuer, 1889, used a forced flap to provide mucous membrane and cervical flap for the skin surface. Schlimmelsch, 1894, reversed this order using the skin surface of a long cervical flap for mucous and a flap from the neck for the external surface.

Laurenstein, 1893, made use of a long flap from the anterior chest. A bridge of skin and subcutaneous tissue was raised from the midline over the sternum, the incisions being vertical. A second hinged flap was then outlined in a transverse direction at the lower end of the vertical flap, the pedicle of the transverse flap being placed near the margin of the long vertical flap. This second flap was turned under the vertical flap to give its raw surface a covering of skin. The distal end of the long flap with skin on both surfaces could then be freed at a later time and implanted into the defect of the cheek. Esmarch, 1899, reported a defect of the cheek involving the angle of the mouth by using two flaps, both from the face, one raised at the upper margin of the defect and the

other at the lower. The two flaps were then brought together over the defect, completely closing it. Mucous membrane sufficient to cover the inner surface was secured by undermining the mucosa from adjacent parts.

Horsley, 1915, lined the cheek with a flap from the neck which was inserted into the mouth through an incision made between the mandible and the overlying soft parts. A suitably shaped forehead flap nourished by a pedicle of subcutaneous tissue containing the anterior temporal artery was used for the external covering. The use of a pedicle of subcutaneous tissue reduced the scarring of the face to a minimum. Esser, 1917, and Imre, 1921, practiced a method whereby large flaps were raised from the vicinity of the defect and rotated, or otherwise moved into position. Davis, 1919, employed a large pedunculated flap raised from the outer surface of the arm with its base in the midthigh region. The distal end of the flap was folded upon itself bringing raw surfaces together and providing a covering of skin on both sides. Contracture of the flap was prevented by stretching it over a gauze covered wire frame where it was held by sutures. It was transferred to the defect 2 weeks later.

Blair, 1921, obtained a good result by suturing the free end of a long cervical flap into a defect in such a way that the skin surface replaced the missing mucosa. The external covering was secured by gradually unrolling the flap and folding it upon itself. Lexer, 1926, used a flap the pedicle of which was placed in front of the ear and contained the temporal artery. The free end was shaped something like a pistol grip and consisted partly of the skin of the forehead and partly of the hair-bearing adjacent scalp. The hairless forehead skin was turned under to form a substitute for mucous membrane.

The repair of full thickness defects of the cheek with satisfactory restoration of function and appearance is often a painstaking and difficult matter. The number of methods devised is evidence that no completely acceptable solution has been reached. If the defect involves the angle of the mouth and adjacent portions of the lips the problem is still further complicated.

Flaps raised from the areas adjacent to the defect have a good blood supply, resist infection better than tissues brought from more remote sources, and match the surrounding skin in color and texture. Their use, however, results in further scarring of the facial region, and it is often necessary to cover the area from which they have been removed with free grafts which present color contrast with the surrounding skin.

Flaps from more remote areas, such as the chest or arm usually have a relatively poor blood supply and are susceptible to ischemic necrosis or destruction by infection. To be transferred safely, remote flaps must be raised in two or more stages to permit the development of an adequate blood supply, and it is often necessary for the patient to maintain an uncomfortable position during the healing period. They also present color contrasts with the face which are permanent, exhibit a tendency toward lymphedema which may persist for months, and tend to contract into a conspicuous, unsightly mound.

The method about to be described avoids some of the objectionable features of the procedures that have just been reviewed. Its greatest use is for full thickness defects of the cheek involving the angle of the mouth with not more than one third of the adjacent lips and extending not more than half way from the angle of the mouth to the posterior margin of the ascending ramus of the mandible. It is not applicable to larger defects because of the limited amount of skin and mucosa available for repair. The operation is carried out essentially in the following manner.

An incision is begun approximately at a point overlying the junction of the zygomatic process of the temporal bone with the temporal process of the zygomatic bone. The incision is carried posteriorly and downward immediately in front of the ear and then curved in a posterior direction around the lobe of the ear to a point slightly behind the anterior border of the sternocleidomastoid muscle (Fig 4). The incision is then carried downward and forward along the anterior border of this muscle for about two thirds of the length of the muscle. The incision goes through the skin and subcutaneous fat but not into the muscle sheaths because the branches of the facial nerve are in close relationship to the fascia overlying the muscle.

A second similar incision is then begun at a point about 2 centimeters below the inner canthus of the eye. It is carried downward and posteriorly in a direction tangential to the posterior margin of the defect. The line of incision from this point coincides with the posterior, or lateral, border of the defect and is then directed anteriorly and downward crossing the mandible about 1 centimeter lateral to the midpoint of the chin. It is carried medially to the midline and then vertically downward to the thyroid cartilage (Fig 4). Triangles of skin and subcutaneous tissue are then removed above and below the defect, as shown in Figure 4, so that folding will not occur when the flap is subsequently moved for-



Fig. 4.

Case 2. Patient as he appeared before operation. The carcinoma arising from the mucous membrane has extended through the cheek and involved the skin.



Fig. 5.

Case 2. The lesion as it appeared within the mouth.

ward. The incisions just described outline what is essentially a double pedicled flap.

Elevation of this flap is begun at the posterior border and carried forward keeping always external to the fascial sheath of the masseter muscle and at a corresponding depth above and below. When the anterior border of the masseter is reached the incision is made deeper until it passes through the mucous membrane and actually enters

the mouth (Fig. 5). Some of the buccal branches of the facial nerve are divided at this point but no apparent harm results. The mucous membrane is incised close to its gingival reflexion so that almost the entire remnant of mucosa will be included in the midportion of the flap (Fig. 5). Above and below level of mouth the pedicles of flap consist of skin and subcutaneous fat alone, the original level of dissection being maintained.



Fig. 3.

Fig. 3. Defect being created by removal of the cancer. Fig. 4. Drawing illustrating defect left by removal of carcinoma and outline of double pedicled flap used to repair it. At anterior margin of flap triangles of skin and subcutaneous fat have been removed to prevent folding of skin at these points when the flap is moved forward.



Fig. 4.



Fig. 5.

The flap is being elevated from posterior approach. The dissection is carried along plane of fully superficial to the sheath of the underlying muscle is reached. At this point extends depth until the buccal cavity entered.

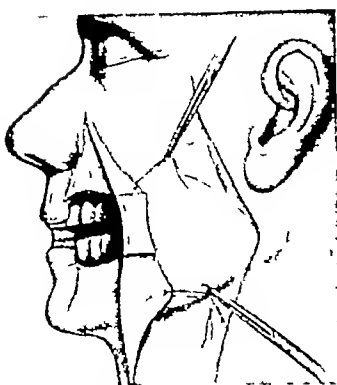


Fig 6



Fig 7

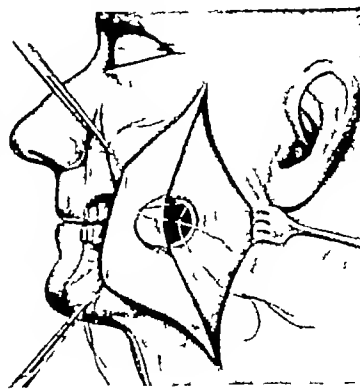


Fig 8

Fig 6 The anterior margin of the flap has been raised in a manner similar to the elevation of the posterior margin. The buccal mucosa is included as a part of the flap. The dotted line indicates the position of the incision made in the underlying mucosa from the posterior approach.

Fig 7 The entire flap has now been raised and is ready to be moved forward into the defect. The underlying

mucosa is an integral part of the flap and is carried forward with it. The position of the patch of mucous membrane on the deep surface is indicated by the dotted line.

Fig 8 A suture has been placed to illustrate the manner of resuturing the mucous membrane. The ties are made within the mouth.

The dissection of the flap is completed from the anterior approach. The pedicles above and below consist of skin and subcutaneous fat, as in the posterior part of the dissection, and mucous membrane is included in midportion (Fig 6).

After the flap has been completely elevated (Fig 7) sutures are placed in the posterior mu-

cosal edges, as indicated in Figure 8, but are not tied until the anterior suture line is completed. The flap is then displaced forward to cover the entire defect. The cut edges of the lips are brought together to form a new angle of mouth, and this in turn is sutured to the anterior border of the flap at the proper level. Closure of the anterior

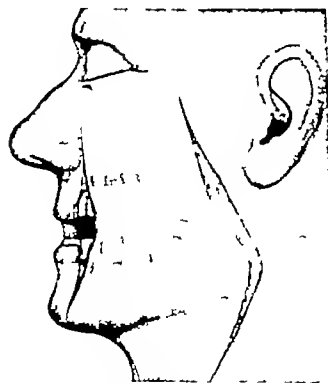


Fig 9

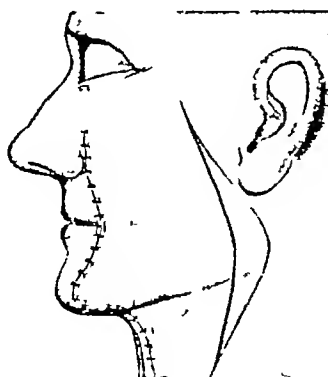


Fig 10



Fig 11

Fig 9 In this transparent illustration the mucosa for the sake of clearness is shown completely resutured except at the anterior margin. In actual practice the posterior mucosal sutures are not tied until the anterior suture line is closed. It appears unnecessary to free completely the area of mucous membrane at its margins and then resuture it but this step is necessary before the natural elasticity of the mucosa can be used to best advantage. The mucous membrane at posterior margin of defect can sometimes be brought together for short distance by simple interrupted sutures thereby reducing size of area to be covered.

Fig 10 The anterior line of incision has been closed with interrupted sutures which go through all layers including the mucous membrane. In those cases in which it is found that the posterior line cannot be completely closed, the residual area may be covered with a free graft of skin.

Fig 11 The posterior suture line is closed as the last step in the operative procedure. The depression which is present below the mandible is due to the removal of the cervical lymph nodes before the flap was sutured in place.





Fig. 2.



Fig. 3.



Fig. 4.

Fig. 2. Front view of patient, 5 years after operation.  
Fig. 3. Lateral view, 5 years after operation. The scars are visible but not particularly conspicuous.

Fig. 4. This photograph is an illustration of moderate asymmetry which is produced when the mouth is opened.

line is completed with interrupted sutures which include the edge of mucous membrane. The upper lower and posterior margins of the mucous membrane comprised in the flap are then re-sutured. It is sutured to the gingival mucosa from which they were cut. The suturing is conducted in part under the posterior half of the flap (Fig. 8) and partly from an anterior approach within the mouth. Usually there is sufficient elasticity to permit complete restoration. If it is necessary to leave a small defect in the mucosa it is preferable to have the deficiency at the posterior angle where healing by granulation will produce minimal interference with function.

After the closure of the anterior suture line, defect in skin and subcutaneous tissue is left at the posterior border of the flap (Fig. 6). By virtue of the elasticity of the skin it is possible as a rule, to close this defect completely by simple interrupted sutures (Fig. 7). In those instances in which complete closure is not possible, the defect which remains may be covered with free graft of skin.

When the loss of tissue has been due to cancer removal of the lymph nodes of the anterior cervical and submental triangles may be carried out 2 weeks after the reconstruction operation by reopening the lower portions of the two suture lines and re-elevating the lower pedicle of the flap. This permits thorough removal of the nodes by dissection without running the risk of serious neck infection.

The operation described has been performed in 3 cases with satisfactory results. In each instance the loss of tissue was due to the removal of an extensive carcinoma.

**CASE J. S.** 41st male, 64 years old, admitted to the Skin and Cancer Unit of the New York Post-Graduate Hospital February 6, 1932 for large carcinoma of 8 months' duration involving the skin and mucous membrane of the cheek at the left angle of the mouth (Fig. 5).

On February 22, 1932, the growth, as measured, the thickness of the cheek and approximately one-third of the upper and lower lips being included. A double pedicle flap of the type here described, as elevated, and direct dissection of the cervical lymph nodes of the anterior and submental triangles of the left neck, as carried out. The flap, as then moved forward and sutured into the defect completely closing it.

On October 9, 1932 an attempt was made to widen the mouth by making a short horizontal incision at the neck. This resulted in the development of small V shaped defects of the upper and lower lips which had to be repaired later.

The functional and cosmetic results were considered good (Figs. 6 & 7). There was no recurrence of carcinoma. The patient died May 24, 1934 of arteriosclerotic heart disease.

**CASE W. S.** 41st male, 47 years old, was admitted to St. Luke Hospital, Newark, N. J. for carcinoma of the left cheek involving the angle of the mouth. On the following day the cancer, as excised, and the defect, as repaired in the manner here described. The cervical nodes were removed at the same operation.

The functional and cosmetic results were satisfactory but when the patient laughed there was slight depression of the left angle of the mouth. This was believed to be due to the fact that at the time of operation an attempt was made to preserve the lower buccal branches of the facial nerve. This apparently resulted in muscular imbalance,

and it appeared probable that a better result would have been obtained if these branches had been disregarded. This patient died April 17, 1933, apparently of carcinoma of the left lung. There was no local or regional recurrence.

CASE 3. I. H., a white male, 67 years old, was admitted to St. Luke's Hospital June 22, 1936, for carcinoma of the left cheek involving the angle of the mouth. The tumor was removed and the defect was repaired by means of a double pedicled flap of the type that has been described.

On July 25, 1936, the lower portions of the suture lines were reopened, the lower pedicle of the original graft was elevated and through this approach a block dissection of the lymph nodes of the submental and anterior cervical triangles was done.

The wounds healed by primary union following both operations. The cosmetic and functional results were good and there has been no recurrence of the tumor.

### ANALYSIS OF RESULTS

There were no serious complications in any of the cases, even though the primary operations in Cases 1 and 2 included cervical lymph node dissections in addition to removal of the primary tumor and repair of the defect. Better cosmetic results were obtained in the 2 cases in which no attempt was made to avoid the facial nerve fibers encountered at the anterior border of the masseter than in the one case in which a part of the fibers were spared. From the experience with Case 1 it appears inadvisable to attempt to widen the mouth by surgical means. Better results were obtained in Cases 2 and 3, and this was not done.

In cases of carcinoma, cervical node dissection can be done either at the time of repair or subsequent to it.

**Advantages.** From the limited experience with the type of repair that has been described certain advantages are apparent:

1. The repair is a one stage procedure, and healing by primary union may be reasonably expected. Multiple operations and a long period of hospitalization are avoided.
2. The two pedicles of the flap insure a good blood supply and greater resistance to infection.
3. The scars largely follow the natural lines of the face and within a few months become relatively inconspicuous.
4. The repair is made with skin and tissues which are a part of the face and the cosmetic result is not marred by color contrasts.
5. The general symmetry of the face is preserved when the face is at rest. Only slight distortion occurs during emotional expressions and when the mouth is opened widely.
6. No serious scar contractures occur following the operation. The upward and downward pulls tend to neutralize each other and the position of the angle of the mouth remains at the same level. The contracture in a lateral direction simply

tends to widen the mouth which has been made narrow by the operation.

7. If the defect has been due to removal of cancer, a subsequent upper cervical node dissection can be done without creation of more scars.

**Disadvantages.** To be weighed against the advantages of the operation there are certain disadvantages which must be considered:

1. It involves some transverse narrowing of the mouth.
2. When the patient smiles or opens the mouth widely some asymmetry is apparent (Fig. 14).
3. The operation necessitates the making of additional scars on the face.
4. The method is not applicable to very large defects, and cannot be used if there has been extensive damage to the skin or mucosa adjacent to the defect. If the operation is restricted to the cases in which it is applicable, its advantages appear to outweigh its disadvantages. This conclusion is strengthened by a consideration of other methods available for the repair of such defects.

### SUMMARY

A method of repairing full thickness defects of the cheek involving the angle of the mouth and adjacent portions of the lips is described.

Its advantages and disadvantages are discussed and the results in specific cases are presented.

It is applicable to moderate sized full thickness defects in the region indicated.

### REFERENCES

1. BARDENHEIMER, B. Deut. med. Wschr., 1891, 17, 773-774.
2. BLAIR, V. P. Surg. Gyn. Obst., 1921, 33, 261-272.
3. CZERNY, V. Beitr. klin. Chir., 1899, 4, 621-624.
4. D'AMMON, F. A., and BAUMGARTEN, M. Chirurgie Plastique. Gand 1 and E. Gyselynek, 1843.
5. DAVIS, J. S. Plastic Surgery. Pp. 581-584. Philadelphia: P. Blakiston's Son & Co., 1919.
6. FESMARCH, F., and KOWALZIC, F. Chirurgische Technik. Kiel and Leipzig: Lipsius & Tischer, 1899.
7. FESSER, J. F. Ann. Surg., 1917, 65, 297-315.
8. GERSONY, R. Zbl. Chir., 1887, 14, 706-708.
9. GUSSENBAUER, C. Arch. klin. Chir., 1877, 21, 526-536.
10. Idem. Prag. med. Wschr., 1885, 10, 117-119.
11. HAHN, L. Verh. Deut. Ges. Chir., 1887, 16, 102-203.
12. HORSLEY, J. S. Am. M. Ass., 1915, 64, 408-410.
13. IMRF, J. J. Am. M. Ass., 1921, 76, 1203-1207.
14. ISRAEL, J. Arch. klin. Chir., 1887, 36, 376-380.
15. KRASKA, P. Zbl. Chir., 1888, 15, 889.
16. LAUFENSTEIN, C. Verh. Deut. Ges. Chir., 1893, 22, 58-65.
17. Idem. Ann. Surg., 1893, 18, 574-577.
18. LEHRER, I. Bier, Braun, and Kummel. Chirurgische Operationslehre, vol. 1, pp. 444-447, 6th ed. Leipzig: J. A. Barth, 1933.
19. SCHIMMELNUSCH, C. Berl. klin. Wschr., 1892, 29, 1287.
20. VON HACKER, V. R. Zschr. Heilk., 1888, 9, 163-172.

# CERTAIN PLASTIC PROBLEMS IN THE SURGERY OF PERIPHERAL NERVES

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IT is true of most special branches of surgery that sooner or later they interlock and fit one is on the lookout, and knows the potentialities of each branch, the sooner a suitable occasion arises. This paper deals with certain cases in which co-operation with a plastic surgeon (A.B.W.) enables a surgeon in charge of a peripheral nerve unit (J.R.L.) to simplify the problem of repairing peripheral nerves. The special features of these cases are two: (1) the absence of supple skin over the site of injury, to a nerve or (2) the situation of the wound in the skin exactly over the point of division of the nerve, so that if the steps to be described are not taken, two suture lines will be at the same level. In both cases further problems may arise because of sepsis and the deposition of scar tissue, and because of the presence close to the nerve, of tendons which may also have been divided. The principles involved may be illustrated by a case history.

On July 26, 1941, a soldier aged 20 sustained a lacerated wound of the left elbow region, which was dealt with in hospital 5 hours after injury. Road dirt had been ground into the medial epicondyle, and there was extensive laceration of the skin and of the muscles of flexor-pronator group,

with complete severance of the ulnar nerve. The wound was cleaned and explored, and the ends of the ulnar nerve were united with stay sutures and covered as far as possible with muscle. The torn skin was sutured over the nerve, but left open over the rest of the wound. The patient was admitted to hospital as a peripheral nerve case on October 3, 1941, when the wound was still not healed. It presented an irregular puckered scar of roughly kidney shape (Fig. 1). Flexion of the elbow was limited to 120°; 60° of pronation and supination was left.

*Neurological examination.* Flexor carpi ulnaris was at first, as was flexor digitorum profundus to the 5th digit, the remaining muscles innervated by the ulnar nerve were paralyzed. Sensory loss was present over the area supplied by the medial cutaneous nerve of the forearm and the ulnar nerve (Fig. 2). Loss of postural sensation was limited to the 5th digit. There was no radiological evidence of injury to bone.

It was obvious that secondary suture of the nerve was necessary and that this could involve shortening its course by transplantation. However, the presence of unhealthy skin adherent to the medial epicondyle made this impracticable. In addition, it was known that there had been considerable loss of muscle, involving that part of the area of the flexor-pronator group in which it is customary to bury

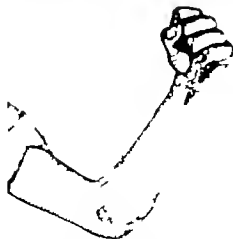


Fig. 1 The scar of the injury just before complete healing. Flexor carpi ulnaris is seen to be contracting.

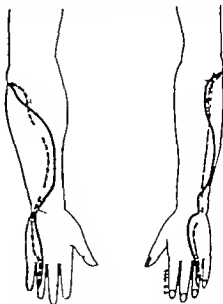


Fig. 2 Area of anaesthesia, November 3, 1941. Cutaneous line, loss to cotton wool, dotted line loss to pin prick.

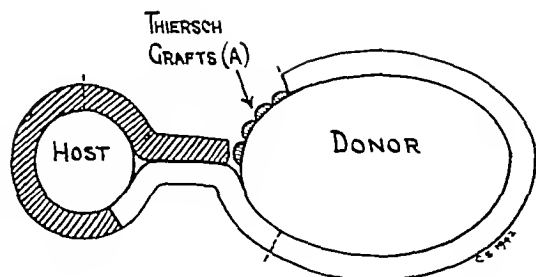


Fig 3 Diagram of first stage of plastic operation

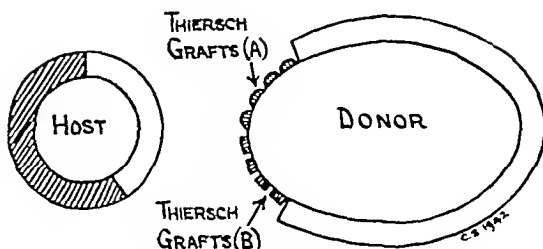


Fig 5 Diagram of final grafting operation

the transplanted nerve. It was decided to arrange first for the replacement of the unsuitable skin, and in the mean time to develop a technique for burying the transplanted nerve more deeply in the limb. Accordingly the patient was transferred to a plastic unit.

From a plastic point of view, the diagnosis was loss of skin and subcutaneous fat on the medial aspect of the left elbow, over an area measuring 10 centimeters by 7.5 centimeters. A pattern of this area was cut in jaconet, and from this a suitable donor area was mapped out on the adjacent thorax and abdomen. At the first operation (A B W) the area of scar on the arm was dissected from its medial boundary to the median line of the scar, and raised as a flap. The anterior half of the donor area was raised as a flap of skin and subcutaneous tissue, hinged posteriorly, and turned so that its (previous) anterior margin could be stitched to the medial margin of the defect in the arm. The remainder of the donor flap received the flap raised from the arm. The raw area of the donor site was covered by a Thiersch graft (Fig 3). Three weeks later a delaying opera-

tion was carried out (A B W) to encourage vascularization from the humeral attachment of the donor flap, under local anesthesia, the donor flap was mapped out from the pattern, raised from the deep fascia except for two small areas at the posterior angles, and stitched back into its previous position (Fig 4). Ten days later, under general anesthesia, the excision of the scar tissue in the arm was completed (A B W) the donor flap completely detached from its original situation and stitched into its new position, and the remaining raw area of the donor site covered by a Thiersch graft (Fig 5). All stitches were removed on the 7th day. The graft took well, except for a small area at its distal and medial edge, where epithelization was completed by a few pinch grafts (Fig 6).

The patient returned to the peripheral nerve unit for secondary suture of the ulnar nerve! on March 22, 1942, after a period of massage to the graft. On this date the neurological examination showed certain differences from that carried out on admission. Postural sensibility had been recovered in the 5th digit, except at the terminal joint, although the part of flexor digitorum profundus acting on the 4th and 5th digits was not now active. The patient felt and localized a pinch on the analgesic border of the hypothenar eminence, and it was of great interest that the upper portion of the skin graft had recovered some sensation (Fig 7).

At operation on March 26, 1942 (J R L) the incision (Fig 8) exposed the ulnar nerve in the arm and then joined the edge of the skin graft so as to leave no acute angle, followed the medial edge of the graft to its distal end, and then diverged along the course of the ulnar nerve, the small area at the lower end of the graft, which had been completed by pinch grafts, was excised. The graft was then turned laterally over the elbow joint and found to be well vascularized and bleeding freely. The ulnar nerve was

Learmonth J R. A Technique for Transplanting the Ulnar Nerve. Surg. Gyn. Obst. 1942; 75: 792.

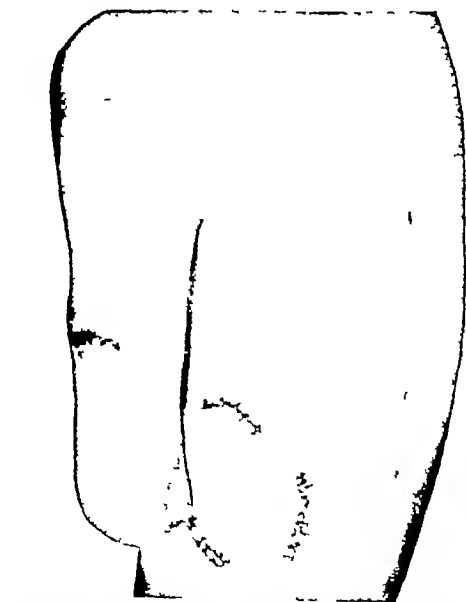


Fig 4 Appearance after delaying plastic operation. The flap is connected to the donor area at its posterior corners only.



Fig 6 The graft in position, and healed

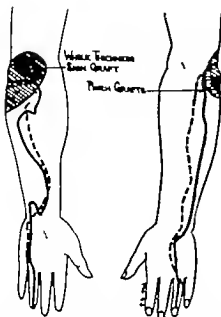


Fig. 7. Area of anesthesia, March, 1925. Note that sensation has returned over the proximal part of the graft. Continuous line, loss to cotton wool; dotted line, loss to pain-prick.

freed from its groove, a distance of 1 centimeter below the epicondyle, and in doing so, branch to the elbow joint and one branch to flexor carpi ulnaris, were sacrificed. Below this level the nerve, as involved in dense scar tissue as it passed between the two heads of flexor carpi ulnaris. The dissection, as therefore transferred to the distal part of the incision, and carried proximally until scar tissue was again reached. The neuroma, as 6 centimeters long and had maximum diameter of 3 centimeters. It was extremely hard in consistence and had united firmly to scraps of muscle in the neighborhood. A tunnel was now made by passing a hemostat under the flexor pronator origin, the nerve, as divided distal to the neuroma and drawn through the tunnel from above downward. As it

is clear that the suture line could lie under the muscles, and as their superficial layers are extensively scarred, it is thought best to resort to the technique which had been elaborated, and to detach the flexor-pronator group from the medial epicondyle. The ulnar nerve could then be placed beside the median nerve, in the depths of the oval. In an intermuscular plane providing the most favorable conditions for suture, so important are the advantages of this procedure that it has been adopted as the routine

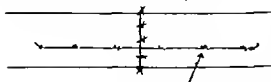


Fig. 9. Epineural tension stitches. One, two, or three may be used. Arrow indicates small bite in epineural sheath.



Fig. 8. Arm after secondary nerve suture. Note placement of incision to avoid acute angles with the edge of the graft, and healing without any loss of graft.

operation for tardy ulnar palsy in all subsequent cases. Suture of the nerve, as carried out with fine black silk with epineural tension stitches used in the wrist as epineuritis, these long gaps have to be overcome (Fig. 6). The flexor pronator group of muscles, as then sutured back into position, with interrupted catgut sutures, and the flexor carpi ulnaris trimmed and repaired as completely possible. The wound in the skin came together without tension, and although the graft area looked little pale, there was really no concern about its vitality. The arm was put up in a light plaster with the elbow in 90 degrees flexion and the forearm pronated. On return to the ward, the patient, as given, doses of 5,000 units of antitoxic serum and course of sulfathiazole, as started. The arm was left undisturbed until April 3, 1925, when the plaster was removed. The wound, as found to have healed by primary union, without any loss of graft (Fig. 8). The postoperative of the splint, as reapplied, and on for 6 weeks after the operation.

At this time, when the patient was discharged, the skin, including the graft, was quite healthy and mobile. Extension and flexion at the elbow joint were still restricted, no doubt from primary loss of muscle tissue, but pronation and supination were almost normal. The area of sensory loss remained the same, there being no further recovery of sensation in the graft. An interesting finding was the presence of goose-skin on stimulation by cold in the lower part of the skin graft, in an area in which sensory recovery had not yet begun.

In this case the plastic procedure converted a difficult problem into a simple one. Lacerated wounds about the elbow region are not uncommon, and it is hoped that the plan adopted will commend itself to other surgeons to encounter similar cases.

The wound which divides nerves and possibly tendons at the same level as the skin is seen most often on the anterior aspect of the wrist. In a time it is not often possible to perform primary suture of tendons and nerves, and in many cases the wound has been infected. Thus when deliberate surgery becomes possible, the patient is found to have a thin puckered scar lacking even the modest layer of subcutaneous tissue which suffices



# GASTROILEOSTOMY AND GASTROILEAL ULCER

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THERE are several complications which may follow gastroenterostomy. When a patient who has had a previous gastric operation presents himself with symptoms referable to the gastrointestinal tract, it is well to analyze the complaints carefully with all the possibilities in mind. The syndromes representing gastrojejunitis, gastrojejunal ulcer, malfunctioning gastroenteric stoma, and postoperative gastritis are rather common after gastroenterostomy. More infrequently recurrent ulceration has led to formation of a gastrojejuno-colic fistula, usually after an interval of time has elapsed after operation. A complication which may not be thought of, and to which we again wish to call attention, is the presence of a gastroenteric stoma which is actually gastroileal instead of gastrojejunal. This low anastomosis is the result of a surgical error.

We have found in the literature (7) 6 previously reported instances of gastroileostomy including the 9 cases of Rivers and Wilbur. It is impossible to determine the general incidence of this surgical error because not all such cases may be reported. At the Mayo Clinic approximately one diagnosis of this condition is made in each 10 years.

In the present paper we wish to present 8 additional cases of gastroileostomy and also 1 case in which the patient had been seen previously at the clinic and which was reported by Rivers and Wilbur but not proved surgically until recently. All the operations had been performed prior to the registration of the patients at the clinic and in each instance subsequent confirmatory operation was performed at the clinic.

## REPORT OF CASES

CASE 1. In September 1927, 35 year old Jewish came to the clinic complaining of abdominal pain. In 9 she had begun to notice daily ulcer like pain. Four days after gastroenterostomy had been performed in 9 6, supposedly for duodenal ulcer diarrhea began, with 10 stools daily. After years the frequency of the stools decreased to 4 or 5 daily persisting this way until her registration at the clinic. Frequently identifiable undigested food passed from the bowels 1 1/2 to 2 hours after ingestion. Constant occurred at times and gave relief from an epigastric lacer pain. When seen 9 years after operation the patient had lost 10 pounds (4.5 kgm) dropping from 150

pounds (68.2 kgm) to 140 pounds (63.5 kgm). Her height was 5' 6" (167.6 cm). A free acidity as shown on aspiration of gastric contents after an 8 hour and Roentgenological examination showed an anastomosis between the stomach and the lower part of the ileum, allowing the barium to pass immediately into the large bowel. There was deformity of the duodenal cap. A diagnosis of gastroileostomy was made and surgical treatment was advised. The patient decided not to have operation then.

In July 1934 this patient returned to the clinic with the same complaints. She had not had any surgical treatment for her low anastomosis during the interval. From 1927 to 1934 she had continued to eat every 4 days and to have 10 stools and bricking 10 lbs. odor. Her condition improved between 1930 and 1934 and she gained eight slowly. During the years prior to her last visit to the clinic, colic, loss of weight, and abdominal cramps in each bowel movement developed. In March, 1934, counting suddenly increased and diarrhea above the anastomosis. This distress extended to the back and shoulders. The gall bladder, as not visualized in its cholecystograms elsewhere, and cholecystectomy had been advised. Her weight which had varied 10 pounds with clothing had decreased in the 4 months before admission to 135 pounds without clothing.

Examination showed only slight loss of weight and signs of nutritional deficiencies were remarkable by their absence. Fractional analysis of gastric contents after test meal showed maximal total acidity of 100, 100% free acidity. The total concentration of serum protein measured 5.8 grams per 100 cubic centimeters of blood. An albumin globulin ratio of 2.33. Cholecystography failed to reveal shadow of the gall bladder but this was attributed to poor absorption of dye, resulting from the low anastomosis. Re-examination of the stomach and colon reconfirmed the presence of gastroileal stoma (Fig. 1). The symptoms were of sufficient magnitude to indicate again the need for surgical intervention.

At operation on August 6, 1934, there was no evidence of previous ulceration of the stomach or duodenum. No cholecystitis nor gastroduodenal ulceration as present in the anastomosis, which was located 6 inches (15 cm) from the ileocecal valve. The stoma was about 1 1/2 inches (4 cm) diameter. After disconnection of the anastomosis the organs in the stomach and ileum were closed. The patient had an unremarkable convalescence. Subsequent fractional analysis of gastric contents after test meal revealed maximal total acidity of 100 and no free acidity.

Even though the anastomosis only 6 inches (15 cm) from the ileocecal valve had been present for 10 years there was no remarkable nutritional deficiency. There was undoubtedly good function of the pylorus. Free acidity and ileal stools had not harmed the patient much. This was Case 8 in the series of Rivers and Wilbur, the only one of that series in which operation was not done at the time.

CASE 2. A 35 year old woman came to the clinic in July 1934, complaining of gas, bloating, diarrhea, colic, and loss of weight. From the age of 15 years she had been subject to sick headaches. In January 1934, after 18 months of indigestion such as associated with the headaches, an operation for exploration of her gall bladder and stomach

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had been performed. The appendix had been removed and a gastroenteric stoma had been established. Immediately after operation diarrhea with frequent bulky and greasy stools had developed. Gas and borborygmus bothered her much. At times she saw undigested food in her stools. There had been a loss of 25 pounds (11.3 kgm) in the period following operation.

Examination revealed marked loss of weight. The abdomen was distended, and peristalsis was visible in some what distended loops of bowel. A test meal showed a total acidity of 4 and no free hydrochloric acid. There was a great excess of neutral fat in the stools. Test of pancreatic secretion showed digestion of casein and starch to be deficient. No roentgenological examination was made.

At operation it was found that the gastroenteric stoma had been made more than halfway down the small intestine, a loop of the upper part of the ileum having been used. The pancreas was thickened and covered with dilated vessels. The gall bladder was large and could not be emptied. After the gastroileal stoma had been disconnected, cholecystostomy was performed. Recovery was uneventful.

In a letter written in February, 1913, the patient stated that she had gained 1 pound (0.5 kgm) a day for 40 days after the operation. She had not been relieved of moderate difficulties with sour stomach.

There was fairly good evidence that chronic pancreatitis with deficient pancreatic secretion played a part in the production of the patient's loose stools. The short circuit of stomach to the upper part of the ileum undoubtedly accounted for most of the symptoms, since her diarrhea disappeared and gain of weight was prompt after operation.

CASE 3. In January, 1922, a 53 year old woman complained of diarrhea and weight loss. From 1906 she had had distress of ulcer type and in August, 1916, roentgenological examination here had demonstrated a duodenal ulcer. A test meal at that time showed total acidity of 36 and free hydrochloric acid of 28. Because of progression of symptoms gastroenterostomy had been performed in March, 1921. Pain was relieved by operation, but as soon as she began to eat solid food diarrhea with 5 to 20 movements a day appeared. The stools often had a lenticular character and prunes could be seen in the stool within 3 hours after their ingestion. Periods of diarrhea lasting about 4 days alternated with periods of fairly normal stools lasting about 6 days. Once after operation she had vomited feces like material and twice had had eructation of the same material. Her abdomen became sore during bouts of diarrhea. She had lost 36 pounds (16.3 kgm) in the 9 months after operation.

Physical examination showed only loss of weight and slight tenderness in the lower part of the abdomen. Analysis of gastric contents by the fractional method showed an acidity until 8 units of free hydrochloric acid appeared after 134 hours, 95 cubic centimeters was recovered. Hemoglobin measured 74 per cent (11.2 gm) per 100 cubic centimeters. Roentgenological examination showed a gastroenteric stoma with communication of small bowel with right half of colon. The duodenal cap was deformed.

At operation the stomach was found to be anastomosed to the ileum only 4 inches (10 cm.) from the ileocecal valve. A chronic ulcer had caused extensive contraction of the duodenum. Accordingly, after disconnection of the gastroileal stoma and closure of the openings, gastrojejunostomy was performed. Two weeks later because of symptoms suggesting obstruction re-exploration was performed. Aside from a mild linking of the bowel at one point nothing of great significance was found. The patient made a good recovery.

In a letter written in November, 1934, the patient stated that she had had no more illness since her operation.

CASE 4. A 37 year old marble worker in August, 1930, complained of swelling of his legs and ankles and of stomach trouble. About 1917 periodic bouts of pain had led to roentgenological examination which had indicated the presence of a duodenal ulcer. In 1927 gastroenterostomy, appendectomy, and cholecystectomy had been performed. After the operation there was no more pain but 8 months later intermittent nocturnal attacks of vomiting developed, coming approximately every 3 weeks and lasting about 1 week at a time. Three to 4 quarts (3 to 4 liters) of greenish material, sometimes containing retained undigested food, would be brought up with good relief of nausea. No diarrhea or fecal belching had occurred. Constipation required a nightly laxative. The patient had lost about 6 pounds (2.7 kgm) in the 4 weeks before admission. About 1 year after operation weakness and stiffness of the legs had developed with associated numbness and tingling up to the knees. Similar numbness was present in the fingers. Sensitivity of the muscles of the arms and legs later led to the use of crutches. Dependent edema was present daily but disappeared at night.

Examination showed loss of weight, dependent edema, and multiple peripheral neuritis. Analysis of gastric contents disclosed a total acidity of 76 units with free hydrochloric acid of 58, 245 cubic centimeters was aspirated. Roentgenological studies showed a low, malfunctioning gastroenteric stoma with retention. There was a secondary type of anemia. A bromsulfalein test of liver function did not show any retention of dye. Serum protein measured 6.5 grams per 100 cubic centimeters of blood.

At operation the anastomosis was found to be between the stomach and a loop of the upper part of the ileum. Because of scarring and contraction below the pylorus, reconstruction of the pyloric outlet was performed after disconnection of the gastroileal stoma. There was no gastroileal ulceration, but the proximal part of the intestine was much distended and the walls were thickened.

The patient stated in a letter in 1934 that he had not been relieved completely by operation and had had some recurrence of pain, perhaps of ulcer type. It is probable that the multiple neuritis in this case was the result of vitamin deficiencies created by vomiting.

CASE 5. A 56 year old railroad section foreman in January, 1936, complained of stomach trouble and external drainage of bile. After an onset of symptoms at the age of 36 (1916) he had had distress of ulcer type mingled with gall stone colics. In 1928, after pyloric obstruction, the gall bladder had been drained and many stones had been removed. Gastroenterostomy had been performed because of an obstruction produced by a duodenal ulcer. Operation relieved him and he gained weight for 6 to 8 months. Recurrent symptoms at that time consisted of burning crampy pain which was referred to the lower part of the abdomen or was generalized. For 7 years the patient had endured this pain, with only partial relief by milk or alkali. In 1935 he found that 2 to 5 hours after meals there would be fullness, then gas, burning, cramps, nausea, and bitter vomiting. At reoperation in July, 1935, narrowing of the gastroenteric stoma had been found. For reasons unknown to us the gall bladder had been drained and a "lump" removed from the stomach. Bile persistently drained externally after this operation, and there was a progressive loss of strength together with a loss of 36 pounds (16.3 kgm) before his admission to the clinic.

At the time of the patient's registration at the clinic, the chief complaints were of cramping, burning pain referred to the lower part of the abdomen, vomiting, marked loss of strength and weight since his second operation, and external drainage of bile together with acholic stools and dark urine.





Fig. Gastrojejunal stomach.

The patient's condition as poor. He was emaciated and dehydrated and had severe abdominal pain. Bile was draining from an external biliary fistula. On roentgenoscopic examination of the stomach, gastrojejunal ulcer with diffuse jejunitis as felt to be present, together with deformity of the duodenal cap and some dilatation of the stomach. An E. acid test result showed total acidity of 60 units and free hydrochloric acid as 50.00 cubic centimeters as recovered.

At operation there were found an anterior gastrojejunal stomach with gastrojejunal ulcer, healed duodenal ulcer which had practically occluded the duodenum, and biliary fistula which communicated with functionless gall bladder. The gastrojejunal ulcer situated on the posterior wall had crater about 5 centimeters in diameter and both afferent and efferent loops of ileum had contracted as result of fibrosis. The gall bladder which did not contain any stones, was removed. The common bile duct as normal. The gastrojejunal anastomosis as disconnected and the gastrojejunal ulcer as excised. A large gastrojejunal stomach as made and temporary jejunostomy for feeding purposes established. The patient made good recovery.

CASE 6. I March, 1937. 6 year old retired fiscal director complained of vomiting. In 1918 he had first noticed epigastric distress of ulcer type. Hematemesis and tarry stools occurred in 1920, and in 1930 milder episode of bleeding occurred. Thereafter on medical regimen he got along. All stool 1936 had mucus and retention type vomiting were shown by roentgenological examinations to be due to pyloric obstruction. Gastroenterostomy had been performed in January, 1937.

Immediately after operation diarrhea had begun, with 6-8 stools daily for about 6 weeks. Undigested food as seen in the stools. The use of bismuth seemed to check the diarrhea but nausea, gagging, and vomiting or regurgitation followed its use. Pain or soreness as present just above the navel in periods varying from several minutes to hours. There was no definite relation of pain to

intake of food but relief could follow power of tea. The patient had lost 60 pounds (27.2 kgm.) in the 3 months after operation.

Examination here showed loss of weight, dryness and slight epigastric tenderness. Analysis of gastric contents showed total acidity of 40 units and free hydrochloric acid of 30.00 cubic centimeters was present. Chemical examination of the blood did not disclose any abnormality. There as no anastomosis. Roentgenographic studies of the stomach showed gastrojejunal stenosis with extensive gastrojejunitis, especially evident at the anastomosis. The gastroenteric stomach had been made with 10 cent of ileum 10 inches (25 cm.) from the ileocecal valve.

At operation it as found that the gastrojejunal stomach had gastrojejunal ulcer by centimeter. Adules performing duodenal ulcer with stenosis at the level of the pancreas had shut off the duodenum almost completely. Because partial gastrectomy did not seem safe, division of the anastomosis as performed with closure of the gastrojejunal ulcer and establishment of an anterior jejunal stomach after closure of the opening in the ileum. Recovery after operation as uneventful. At 10th post meal 24 days after operation showed total acidity of 50 units and free hydrochloric acid of 40.00 cubic centimeters was recovered.

Seven months after operation the patient stated better that he had regained about 10 pounds (4.5 kgm.) and had good strength, good appetite and no pain.

CASE 7. A 53 year old man in June, 1937, gave as chief complaint intermittent pain and gaseous distress below the navel present for 3 years. Prior to 1937 he had growing abdominal distress immediately after gastroenterostomy in 1915 he apparently had been quite well and had had loose stools containing undigested food, but he had been neglected as little as 3 months before. Subsequent symptoms had occurred in bouts of 4 to 6 weeks duration with free intervals of 1 to 2 weeks continuing throughout the 3 years before the patient's registration at the clinic. When he ate, his abdomen as usually comfortable but after breakfast, distention and localized paroxysmal pain at or just below the navel could appear usually about 15 minutes. Ingestion of alkalis and food could not seem to distress. Passage of occasionally large amounts of flatus, 5 or 10 without loose stool containing undigested food, and gas almost complete relief for hour. The cycle every 6 hourly intervals 8 or 10 times daily and frequently could alter the patient. Nausea might be present but vomiting did not occur. Fecal regurgitation or food back had never been noticed. Weight could be lost during spell but regained during the free interval. The patient had lost 7 pounds (3.1 kgm.) in the 3 months just before his visit to the clinic.

Physical examination showed moderate hyperacidity. Observations suggestive of gastroenterostomy at the level of roentgenoscopic examination of the colon were confirmed on roentgenographic examination of the stomach, showed an anastomosis between the stomach and the ileum as apparently about 1 foot (30 cm.) above the ileocecal valve. The duodenum did not seem abnormal. Analysis of gastric contents as not performed.

At operation the anastomosis as found to be about 10 inches (25 cm.) above the ileocecal valve. It was large enough to admit the tips of 4 fingers. No distal anastomosis could be demonstrated. No evidence of duodenal ulcer was demonstrated. The gastrojejunal anastomosis as disconnected and the opening in the stomach and ileum were closed. Recovery as uneventful.

Approximately 1 year after operation examination showed the patient to be in excellent condition with no loss of hypertension. His only complaint as an epigastric bur-

ing when he was tired or nervous. Aspiration of the contents of the fasting stomach showed a total acidity of 8 units and no free hydrochloric acid. Roentgenoscopic examination showed an ulcer type of duodenal deformity.

That this patient was able to tolerate a gastroileal stoma only 12 inches (30 cm) from his cecum for 23 years was undoubtedly due to the fact that his duodenum was normal. This of course permitted enough absorption of food in the upper part of the small bowel to prevent significant loss of weight.

CASE 8. A 34 year old salesman on July 24, 1939, complained chiefly of abdominal pain. In 1923 he had started having episodes of ulcer like distress. In 1924 after heavy exertion an acute perforation of a duodenal ulcer had occurred and required surgical closure. After 9 months' convalescence the patient was relatively free of pain for 5 years except for short bouts of mild ulcer type once or twice a year. After a recurrence of pain in 1930 he had ulcer pain each year until 1937, at which time posterior extension of pain, nocturnal pain, a few days of tarry stools and one attack of vomiting occurred. Gastroenterostomy in May, 1937, had provided complete relief of symptoms until their recurrence in November, 1937, when there were 3 essential differences: (1) There had been a shift of the pain from the epigastric to the umbilical region; (2) extension of pain also had shifted posteriorly to the low lumbar region; (3) pain was accompanied by a distressed full feeling, relieved by one or two enemas daily. Night pain tended to occur earlier. Periodicity and modes of relief were unchanged. There had been a loss of weight of only 5 pounds (2.3 kgm.).

Tenderness was present just above the umbilicus. Analysis of gastric contents showed a total acidity of 84 units and free hydrochloric acid of 74, 150 cubic centimeters were recovered. Roentgenological study showed a duodenal deformity with some obstruction but the pylorus was patent. The gastroenteric stoma was small and, although the anastomosis was free, what was thought to be jejunitis was demonstrated.

At operation there was constriction of the old region of duodenal ulcer, with induration into the head of the pancreas and some obstruction. The gastroileal anastomosis was at a point in the small bowel at least 8 feet (243 cm) distal to the ligament of Treitz. When this was disconnected a small ileal ulcer was found at the base of the mesentery just opposite a contracted stoma. The ulcer was excised and the ileal opening closed. Partial gastrectomy of the Polya type was performed with removal of about half of the stomach. Recovery was uneventful.

A letter from the patient approximately 2 years after operation revealed that he was in good condition, did not have any distress and had increased his weight by 6 pounds.

The shift of pain to a lower point in the abdomen and the relief by enemas were characteristic of ileal ulceration.

CASE 9. A 58 year old farmer in June, 1941, complained of diarrhea. In 1913 he had had an isolated period of what was probably ulcer distress. During 5 months of 1932 symptoms recurred, this time diagnosed as due to ulcer. From 1935 to 1939 about 5 brief bouts of ulcer pain occurred. In February, 1939, acute perforation of a duodenal ulcer had required surgical closure, which had relieved his symptoms until May 20, 1940, when acute perforation again had required surgical closure. As a prophylactic procedure partial gastrectomy had been performed on December 27, 1940. The patient was able to go home in January, 1941, but after 1 month he lost his appetite and diarrhea developed with 6 to 12 loose to watery stools daily. These were scattered throughout the day, but he always had a bowel movement as soon as he ate. Occasionally undigested food could be seen in the stools. He was repelled

by the sight of food and had lost 60 pounds (27.2 kgm) between operation and time of his admission to clinic.

Physical examination showed moderate emaciation, dry skin and slight edema of the ankles. Analysis of gastric contents showed a total acidity of 16 units but no free hydrochloric acid, there was a fetid odor of bile to the 110 cubic centimeters recovered. Total serum protein measured 5.6 grams per 100 cubic centimeters of blood with an albumin globulin ratio of 1:1. Several specimens of stool showed fat, undigested food and meat fibers in excess of normal. Roentgenological studies showed a posterior Polya type of resection, the anastomosis apparently made with a loop of ileum. Barium had passed into the transverse colon and splenic flexure  $1\frac{1}{4}$  hours after the stomach examination.

Surgical exploration showed that at the last operation the remaining portion of the stomach had been anastomosed to the terminal portion of the ileum about 18 inches (46 cm) above the ileocecal valve. There was no gastroileal ulcer. After disconnection of the anastomosis the opening in the ileum was closed, a small cuff of stomach was excised, and the gastric stump was joined to a proximal loop of jejunum in a posterior colic type of anastomosis. Recovery was uneventful. Serum protein measured 4.9 grams per 100 cubic centimeters of blood just before the patient's dismissal, and edema of the ankles was present.

In a letter 1 month after the patient's dismissal his daughter stated that he was doing well except for easy fatigue and no especial gain in weight. Diarrhea had not returned.

This was the only case in which previous partial gastrectomy had been performed.

The symptoms of gastroileal stoma are dependent chiefly on the location of the anastomosis and on whether or not ulceration is present.

Diarrhea was present in 6 of the 9 cases reported in this paper. In 5 of these it began immediately or within a few days after operation. In the 6th case a month elapsed before diarrhea appeared. The henteric character of the stools was indistinguishable from that seen in cases of gastro-jejuno-colic fistula, but the latter would be unlikely as a cause of symptoms coming so soon after operation, a point which is of diagnostic value. Of the 3 other patients in the series 2 with upper ileal anastomoses had had vomiting. One interesting feature is that with but one exception (Case 2) diarrhea occurred only in those cases in which the anastomosis was very close to the large bowel. In 2 of the cases in which anastomosis was very close to the cecum, fecal belching occurred. Diarrhea coming quickly after operation is the chief reason for suspecting a gastroileal stoma. Epidemic diarrhea or postoperative ulcerative colitis might be confusing but cultures of stools and proctoscopic examinations help to distinguish these when seen early. Later these can be excluded rather accurately on the basis of the patient's history.

Vomiting may be of retention type and occasionally has a fecal quality or is accompanied by a belch with fecal odor.

*Loss of weight* may be severe and usually can be attributed to loss of partially digested food in the benteric stools before adequate absorption occurs. Except for Case 5 significant loss of weight occurred in those cases in which there was diarrhea. This loss of weight probably would have been much more severe if there had not been some passage of food through the pylorus.

*Pain* in association with gastrojejunostomy may be of bowel type or of ulcer type. The former is usually lower abdominal and of cramping type with relief on passage of flatus, stool, or an enema. The pain of ulcer type may be burning or cramping and may be referred to the umbilical region or lower abdominal quadrants in much the same fashion as is the pain of gastrojejunal ulcer. Ulcer sequence and neutralization relief are atypical, however. When pain as a symptom is present the chances of finding a gastroduodenal ulcer or gastroileitis are good only when a significant amount of free hydrochloric acid is present on analysis of gastric contents. In 9 of the 10 cases thus far reported in which there was either gastroduodenal ulcer or gastroileitis, values of free hydrochloric acid obtained after Ewald test meals ranged from 30 to 74 units. In the other case analysis of gastric contents was not performed. In the 4 cases thus far reported in which there was free acid on analysis of gastric contents but no ulceration, the concentration was less than 30 units. Eight of the patients who had gastroduodenal ulcer were men, 1 was a woman, and the sex of the 1 remaining was not mentioned. All patients who had gastroduodenal ulcer had had peptic ulcer before operation.

Aside from the complications of gastroileitis and gastroduodenal ulcer patients who have gastrojejunostomy may be subject to nutritional deficiencies. In our series nutritional edema associated with hypoproteinemia, and multiple neuritis occurred. The external biliary fistula in Case 5 was apparently the result of an additional surgical error.

The diagnosis of gastrojejunostomy should be suspected if there is a history of onset of diarrhea very soon after gastroenterostomy. If the stools are benteric and are accompanied by loss of weight, the possibility becomes strong. Vomiting and fecal belching may or may not be present. Roentgenological examination is of the greatest value in making the diagnosis.

If a gastroduodenal stoma is diagnosed and pain similar to that present with gastrojejunal ulcer exists, a gastroduodenal ulcer may be suspected. If the patient is a man, if he had an ulcer before his operation and now has free hydrochloric acid in

greater concentration than 30 units after stimulation by a test meal, the chances are that either gastroileitis or frank gastroduodenal ulcer is present.

Treatment of gastrojejunostomy and gastroduodenal ulcer is surgical. The procedure used opens a course on satisfying the requirements of restoring adequate gastrointestinal continuity and of correcting the primary problem. Part of this may be accomplished by disconnection of the stomach anastomosis and excision of any gastroduodenal ulcer. If the duodenum is normal nothing further can be required. If the duodenum shows evidence of healed or active ulceration, gastrojejunostomy may be sufficient. However if either duodenal or gastroduodenal ulcers are active and secretion of free hydrochloric acid by the stomach is significant, it may be wise for the surgeon to consider partial gastrectomy. The prophylactic value of this procedure must be weighed against the added risk imposed, especially if the patient's general condition has been depleted by the gastrojejunostomy.

#### SUMMARY

Gastrojejunostomy must be considered among the possible causes of symptoms occurring after gastroenterostomy. This type of anastomosis occurs as a surgical error. The cardinal symptoms of its gastrojejunostomy syndrome are diarrhea, vomiting, loss of weight, and pain. Diarrhea characteristically begins soon after operation and often is benteric in type. Vomiting occasionally has a fecal quality. Loss of weight varies with the severity of diarrhea, pain is of bowel type when mixed with that of gastroileitis or gastroduodenal ulcer.

Gastroileitis and gastroduodenal ulcers may simulate gastrojejunostomy ulcer clinically. They are present only when concentration of free acid is significant.

We have reported 8 cases of gastrojejunostomy and also 1 case previously reported but only recently confirmed surgically. Gastroileitis was present in 1 case and gastroduodenal ulcer in 3 cases in our series.

#### REFERENCES

1. EUSTERMAR, G. B. and BALFOUR, D. C. *The Stomach and Duodenum*. Pp. 320-324. Philadelphia: W. B. Saunders Co. 1935.
2. KLEIN, EUGENE. *Arch. Surg.* 1945, 71:77-79.
3. KOGUT, BENJAMIN, and STEIN, EPHRAIM. *Am. J. Surg.* 1945, 71: 867-869.
4. JORD. Quoted by Kogut, Benjamin, and Stein, Ephraim.
5. MARTIN, FRANK, and CARROLL, A. H. *Ann. Surg.* 1915, 61: 557-560.
6. MARTIN, W. H. Quoted by Kogut, Benjamin, and Stein, Ephraim.
7. RYMER, A. B. and WELSH, D. L. *Surg. Gyn. Obst.* 1937, 64: 937-944.

# PLASMA VITAMIN C AND PROTHROMBIN CONCENTRATION IN PREGNANCY AND IN THREATENED, SPONTANEOUS, AND HABITUAL ABORTION

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**A**NTEPARTUM bleeding occurs in early pregnancy with sufficient frequency to warrant consideration from every possible angle. Rutherford reported an incidence of 5 per cent in 1942. Of 24,289 pregnant women admitted to the Woman's Clinic of the New York Hospital, 90 per cent had vaginal bleeding, and of this number 1,648, or 1 in 15, suffered from a complete or incomplete abortion. Of the latter group, 59, or 3.6 per cent, were in the habitual abortion group, and were so designated because of 3 consecutive abortions, following the suggestion of Malpas. The incidence of habitual abortion was 1 in 411. The incidence of threatened abortion in this group of patients was 1 in 55. Therefore, antepartum bleeding in the first trimester of pregnancy is an important problem in itself, particularly so because of the unsatisfactory prognosis with regard to the associated pregnancy.

The underlying causes of the antepartum bleeding are manifold and are given in Table I. As can be seen, organic lesions, as well as other pathological states associated with gestation, require consideration in making a diagnosis of threatened or spontaneous abortion. Attention is directed to the large number of patients in the "undetermined" group. These causes, together with others, are illustrated in Figure 1.

Clinically, most abortions begin with painless bleeding in the second or third month of gestation, which time corresponds approximately to that when the placenta takes over the formation of progesterone. Seldom have the nutritional factors, which may play a rôle in the onset of such abnormal bleeding, been investigated. Evidence is slowly being accumulated which indicates that such bleeding at times may be due to a deficiency in vitamins C and K. It is our purpose to confine this discussion to these 2 vitamins and consider them, together with a nutritional program of adequacy, in the possible prevention of certain types of antepartum bleeding and, therefore, in

the treatment of threatened, spontaneous, and habitual abortion.<sup>1</sup>

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TABLE I—CAUSES OF BLEEDING IN THE FIRST TRIMESTER OF PREGNANCY, INDOOR SERVICE SEPTEMBER 1, 1932, TO DECEMBER 31, 1940

	Total cases
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Erosion or polyp	18
Miyoma	5
Chorioepithelioma	4
Carcinoma of cervix	2
Total	2209
Total number of pregnancies studied	24,289
Incidence of bleeding in first trimester	9.0 per cent

From the Department of Obstetrics and Gynecology, Cornell University Medical College and The New York Hospital.

<sup>1</sup>Presented at a meeting of the Dallas Southern Clinical Society on March 23, 1942, and at a meeting of the New York Academy of Medicine April 29, 1942.

Loss of weight may be severe and usually can be attributed to loss of partially digested food in the lenteric stools before adequate absorption occurs. Except for Case 5 significant loss of weight occurred in those cases in which there was diarrhea. This loss of weight probably would have been much more severe if there had not been some passage of food through the pylorus.

Pain in association with gastrojejunostomy may be of bowel type or of ulcer type. The former is usually lower abdominal and of cramping type with relief on passage of flatus, stool, or an enema. The pain of ulcer type may be burning or cramping and may be referred to the umbilical region or lower abdominal quadrants in much the same fashion as is the pain of gastrojejunal ulcer. Ulcer sequence and neutralization relief are atypical, however. When pain as a symptom is present the chances of finding a gastroduodenal ulcer or gastrojejunitis are good only when a significant amount of free hydrochloric acid is present on analysis of gastric contents. In 9 of the 10 cases thus far reported in which there was either gastroduodenal ulcer or gastrojejunitis, values of free hydrochloric acid obtained after Ewald test meals ranged from 30 to 74 units. In the other case analysis of gastric contents was not performed. In the 4 cases thus far reported in which there was free acid on analysis of gastric contents but no ulceration, the concentration was less than 30 units. Eight of the patients who had gastroduodenal ulcer were men, 1 was a woman, and the sex of the remaining was not mentioned. All patients who had gastroduodenal ulcer had had peptic ulcer before operation.

Aside from the complications of gastrojejunitis and gastroduodenal ulcer patients who have gastroduodenal stomas may be subject to nutritional deficiencies. In our series nutritional edema associated with hypoproteinemia, and multiple neuritis occurred. The external biliary fistula in Case 5 was apparently the result of an additional surgical error.

The diagnosis of gastrojejunostomy should be suspected if there is a history of onset of diarrhea very soon after gastroenterostomy. If the stools are lenteric and are accompanied by loss of weight, the possibility becomes strong. Vomiting and fecal belching may or may not be present. Roentgenological examination is of the greatest value in making the diagnosis.

If gastroduodenal stoma is diagnosed and pain similar to that present with gastrojejunal ulcer exists, a gastroduodenal ulcer may be suspected. If the patient is a man, if he had an ulcer before his operation and now has free hydrochloric acid in

greater concentration than 30 units after stimulation by a test meal, the chances are that either gastrojejunitis or frank gastroduodenal ulcer is present.

Treatment of gastrojejunostomy and gastroduodenal ulcer is surgical. The procedure used depends of course on satisfying the requirements of restoring adequate gastrointestinal continuity and of correcting the primary problem. Part of this may be accomplished by disconnection of the abnormal anastomosis and excision of any gastroduodenal ulcer. If the duodenum is normal nothing further may be required. If the duodenum shows evidence of healed or active ulceration, gastrojejunostomy may be sufficient. However if either duodenal or gastroduodenal ulcers are active and secretion of free hydrochloric acid by the stomach is significant, it may be wise for the surgeon to consider partial gastrectomy. The prophylactic value of the procedure must be weighed against the additional risk imposed, especially if the patient's general condition has been depleted by the gastrojejunostomy.

#### SUMMARY

Gastrojejunostomy must be considered among the possible causes of symptoms occurring after gastroenterostomy. This type of anastomosis occurs as a surgical error. The cardinal symptoms of the gastrojejunostomy syndrome are diarrhea, vomiting, loss of weight, and pain. Diarrhea characteristically begins soon after operation and often is lenteric in type. Vomiting occasionally has a fecal quality; loss of weight varies with the severity of diarrhea. Pain is of bowel type when compared with that of gastrojejunitis or gastroduodenal ulcer.

Gastrojejunitis and gastroduodenal ulcers may simulate gastrojejunostomy clinically. They are present only when concentration of free acid is significant.

We have reported 8 cases of gastrojejunostomy and also 1 case previously reported but only recently confirmed surgically. Gastrojejunitis was present in 1 case and gastroduodenal ulcer in 3 cases in our series.

#### REFERENCES

1. EUTENEIER, G. B., and RALPH, D. C. *The Stomach and Duodenum*. Pp. 820-834. Philadelphia: W. B. Saunders Co. 1935.
2. KLEIN, EUGENE. *Arch. Surg.* 1945, 5: 119-124.
3. KOTTY, BENJAMIN, and STEIN, EPHRAIM. *Am. J. Surg.* 1946, 33: 263-269.
4. JUNG. Quoted by Kogut, Benjamin, and Stein, Ephraim.
5. MARTIN, FRANK, and CARROLL, A. H. *Am. Surg.* 1915, 4: 357-362.
6. MICHOS, W. H. Quoted by Kogut, Benjamin, and Stein, Ephraim.
7. RUTHER, A. B., and WELCH, D. L. *Surg. Gyn. Obst.* 1932, 54: 937-944.

# PLASMA VITAMIN C AND PROTHROMBIN CONCENTRATION IN PREGNANCY AND IN THREATENED, SPONTANEOUS, AND HABITUAL ABORTION

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**A**NTEPARTUM bleeding occurs in early pregnancy with sufficient frequency to warrant consideration from every possible angle. Rutherford reported an incidence of 5 per cent in 1942. Of 24,289 pregnant women admitted to the Woman's Clinic of the New York Hospital, 90 per cent had vaginal bleeding, and of this number 1,648, or 1 in 15, suffered from a complete or incomplete abortion. Of the latter group, 59, or 3.6 per cent, were in the habitual abortion group, and were so designated because of 3 consecutive abortions, following the suggestion of Malpas. The incidence of habitual abortion was 1 in 411. The incidence of threatened abortion in this group of patients was 1 in 55. Therefore, antepartum bleeding in the first trimester of pregnancy is an important problem in itself, particularly so because of the unsatisfactory prognosis with regard to the associated pregnancy.

The underlying causes of the antepartum bleeding are manifold and are given in Table I. As can be seen, organic lesions, as well as other pathological states associated with gestation, require consideration in making a diagnosis of threatened or spontaneous abortion. Attention is directed to the large number of patients in the "undetermined" group. These causes, together with others, are illustrated in Figure 1.

Clinically, most abortions begin with painless bleeding in the second or third month of gestation, which time corresponds approximately to that when the placenta takes over the formation of progesterone. Seldom have the nutritional factors, which may play a rôle in the onset of such abnormal bleeding, been investigated. Evidence is slowly being accumulated which indicates that such bleeding at times may be due to a deficiency in vitamins C and K. It is our purpose to confine this discussion to these 2 vitamins and consider them, together with a nutritional program of adequacy, in the possible prevention of certain types of antepartum bleeding and, therefore, in

the treatment of threatened, spontaneous, and habitual abortion.<sup>1</sup>

What rôle does a deficiency in vitamins C and K play in the production of the bleeding? A perusal of the literature reveals pertinent information. Mendive and Deulofeu have shown that the hypophysis, as well as the thymus, adrenal, spleen, testis, pancreas, and thyroid glands contained large amounts of vitamin C. Biskind and Glick have shown that the corpora lutea of cows contain abundant amounts of vitamin C and suggest a correlation with the production of progesterone. Israel and Meranze found a progesterone-like effect on the endometrium following the administration of ascorbic acid to infantile and ovariectomized rabbits. With regard to abortion, Voght observed that guinea pigs which had been given ascorbic acid frequently aborted. The clinical counterpart of this observation was provided by Ley who treated 10 cases of habitual abortion with success. The recent discovery of the anti-hemorrhagic vitamin K led Singleton to employ it clinically in the form of dehydrated young grasses in cases of abortion, with promising results. Javert found retroplacental hematoma and

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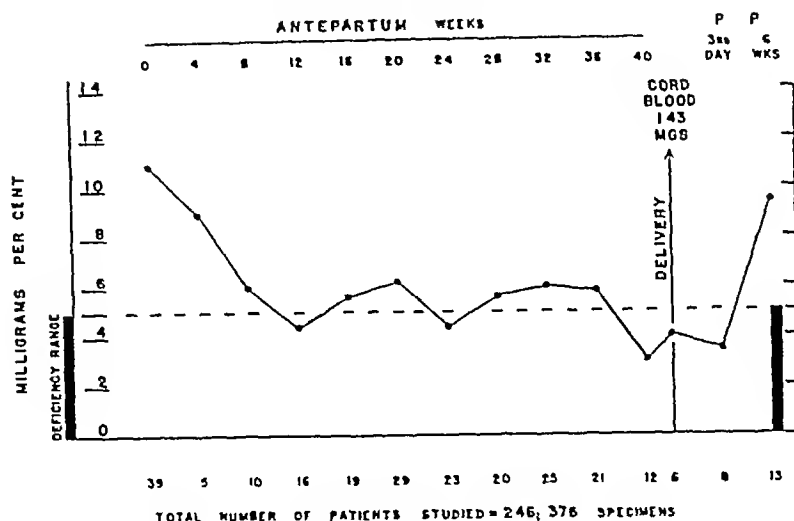


Fig. 3 Plasma vitamin C (ascorbic acid) saturation in normal pregnancy

taining the low concentration in the second and third trimesters of pregnancy since they are also responsible for reduction in the cell volume and hemoglobin, as shown in Figure 5.

At term the maternal plasma contains about 0.4 milligram per cent of ascorbic acid. The values at delivery reported in the literature are at variance with each other. Abt, Farmer, and Epstein obtained an average value of 1.03 milligrams per cent, while Sadosky and Wertheimer obtained a similar value, 1.09 milligrams per cent. Teel, Burke, and Draper reported a value of 0.52 milligram per cent which is more in accord with our own data. On the other hand, cord blood has a much higher concentration, 1.42 milligrams per cent, which compares favorably with the values reported by Teel, Burke, and Draper, Abt and his co-workers, and by Braestrup. It would appear that the maternal stores are depleted to supply the infant, and that the vitamin passes readily through the placenta.

The fetal requirements of vitamin C after birth are also of interest. During the first 10 days of life, there is a decrease from 1.07 milligrams to 0.27 milligrams according to Braestrup. Values ranging from 0.0 to 0.3 milligram were found in several of our infants who developed hemorrhagic disease of the newborn. The prothrombin concentration of these infants was probably very low. Perhaps a deficiency in vitamin C, in addition to hypoprothrombinemia, is necessary for the development of hemorrhagic disease. Javert has recently intimated that a lack of both vitamins C and K may be responsible for this disease

in the newborn, since too many infants have hypoprothrombinemia without hemorrhagic manifestations. This view is borne out in part by the observations of Sanford and his co-workers, who found that infants with cerebral hemorrhage had low blood values for vitamin C.

On the third postpartum day, the blood vitamin C was 0.35 milligram, slightly lower than the value at delivery. The onset of lactation may be responsible for this low value, while wound healing (episiotomies and lacerations), and uterine involution and impaired intake must also be considered as contributory factors. During the first 14 days of lactation, Ingalls, Draper and Teel, and Sadosky and Wertheimer found that breast milk contains from 4.5 to 4.62 milligrams of ascorbic acid per 100 cubic centimeters which is considerably higher than the amount present in the maternal plasma. At 6 weeks postpartum the vitamin C level had returned to normal, as indicated in Figure 3.

The daily oral administration of 100 milligrams of cevitamic acid and 100 cubic centimeters of orange juice to 100 deficient pregnant patients produced a rise in the plasma vitamin C to normal, showing that an adequate supplement will increase the content of this vitamin in the blood. This provides a clue as to the amount of vitamin C required to maintain normal concentration in the blood in pregnancy. Evidently about 200 milligrams is needed daily. Braestrup found that mothers on a deficient diet had vitamin C concentration of only 0.26 milligram per cent. This suggests that our deficient patients were also on



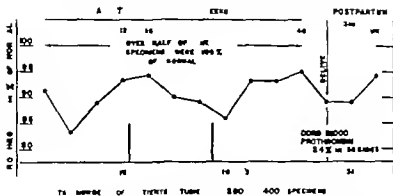


Fig. 4. Plasma prothrombin concentration in normal pregnancy

Inadequate diets despite the fact that their dietary history and economic level were considered satisfactory. Experience has indicated that diet and income do not always have a relation to the blood concentration of vitamin C in pregnancy. Food aberrations, nausea and vomiting common to parturient women, can vitiate the most adequate diet. Therefore, actual determination of vitamin concentration seems to be a better index of saturation or deficiency in pregnancy than the dietary history or the financial status of the patient.

#### PLASMA PROTHROMBIN IN NORMAL PREGNANCY

The plasma prothrombin concentration of 300 normal pregnant women has been discussed elsewhere by Javert and Maciel, and the results are summarized in the curve in Figure 4. Studies of an additional 300 patients show no marked deviation from their original data. The curve has primary and secondary trends; the former is upward while the secondary trends vary with the

trimesters of pregnancy. In the first trimester the prothrombin concentration is lowest, probably due to a deficient intake of vitamin K, "morning sickness," or vomiting. However, the majority of patients (85 per cent) had an average prothrombin concentration ranging from 83 to 96 per cent of normal up to delivery. However, the average for the cord blood was only 24 per cent of normal.

Some of the patients with deficient values in vitamin C and prothrombin complained of bruising easily, epistaxis, bleeding gums, and vaginal bleeding. The latter was sometimes in the nature of a threatened abortion.

#### PLASMA VITAMIN C AND PROTHROMBIN DETERMINATIONS IN ABORTION PATIENTS

Plasma vitamin C and prothrombin determinations were made on 3 groups of patients: those having had either a threatened abortion, 2 or 3 previous spontaneous abortions, or habitual abortions (3 or more consecutively). Seventy-nine patients were studied. Data on these 3 groups of cases are given in Tables II and III. The total

TABLE II.—PLASMA VITAMIN C\* (ASCORBIC ACID) IN PATIENTS WITH THREATENED SPONTANEOUS OR HABITUAL ABORTIONS

Group	Number of cases	Vitamin C in mgm per cent		Deficiency severe or less	
		Average	Range	Number	Percentage
Threatened abortion	30	0.45	0.05-0.81	14	47
Spontaneous abortion	37	24	0.0-0.48	17	
Habitual abortion		34	0.0-0.48	14	41
Total	79	23	0.0-0.48	45	57
Control patients 4-16 weeks pregnant	30	15	0.0-1	25	83

\*McAfee and Butler microtechnique.

TABLE III.—PLASMA PROTHROMBIN CONCENTRATION\* IN PATIENTS WITH ABORTION

Group	Number of cases	Prothrombin concentration per cent of normal		Deficiency severe or less	
		Average	Range	Number	Percentage
Threatened abortion	30	84	7-100	13	43
Spontaneous abortion	37	48	3-100	30	81
Habitual abortion	12	61	3-100	11	92
Total	79	54	3-100	54	68
Control patients 4-16 weeks pregnant	30	92	70-100	2	7

\*Hansen, Brinkman, and Smith technique.

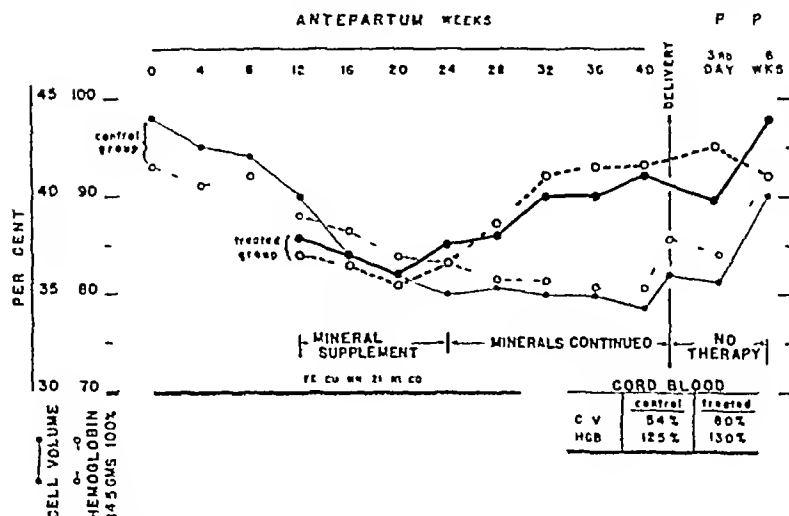


Fig 5 Cell volume and hemoglobin determinations in normal pregnancy in a control group of 200 patients (1,000 determinations) and in a treated group of 8 habitual abortion patients receiving mineral supplement

average value for vitamin C in all of the groups was 0.35 milligram per cent and was definitely lower than that found in normal pregnant patients used as controls. The incidence of vitamin C deficiency was 69 per cent in the abortion patients. The prothrombin concentration was studied in the same groups of abortion patients, and the values are presented in Table III. The average prothrombin concentration was 54 per cent of normal, using the Warner, Brinkhous, and Smith technique. This is considerably below the normal value of 92 per cent observed in the normal control patients. The percentage incidence of prothrombin deficiency was 72 per cent in the abortion group. The relationship of prothrombin concentration to vitamin K (in the absence of liver disease) has been well established. It can be presumed that the abortion patients were deficient in vitamin K, since an elevation in the prothrombin level followed the administration of vitamin K to most of the patients having a low concentration.

Deficiency in both vitamin C and prothrombin (vitamin K) was present in 61 per cent of the patients. The remaining patients, 39 per cent, were low in either one or the other. Seldom did an abortion patient have normal values for both vitamin C and prothrombin. It would appear that deficiency in vitamins C and K plays an etiological rôle in the production of threatened and spontaneous abortion, as intimated above and shown in Figure 2. This deficiency may be the causative factor of the decidual bleeding which

is often the first clinical sign of miscarriage. It seems significant that abortions occur most commonly in the second and third months of gestation when the vitamin C and vitamin K levels have been found to be low.

#### TREATMENT OF ABORTION

The results of clinical application of vitamin C and vitamin K therapy, together with a planned nutritional program of adequacy with regard to other vitamins as well as minerals, have shown considerable promise. In addition to an adequate dietary regimen, it has been our practice to use supplements of vitamin C in the form of fresh grapefruit, orange, lemon, or lime juice. Cevitamic acid, 100 milligrams daily, has been provided in addition when the blood values have been exceedingly low. Vitamin K has been supplied in watercress, spinach, cabbage, cauliflower, and dandelion greens. When the prothrombin concentration has been low, synthetic vitamin K has been given either orally as synkavite (Hoffman-LaRoche), 5 milligrams daily, or intramuscularly in amounts of 2 to 4 milligrams of thyloquinone (Squibb) in order to maintain a normal prothrombin level.

In addition to the above, a mineral supplement called endomin (Reed and Carnrick) has been employed to provide iron, copper, cobalt, nickel, and zinc. The endomin assisted in the prevention of a lowering of the maternal cell volume and hemoglobin that ordinarily is attributed to hydremia of pregnancy, as indicated in Figure 5.

TABLE IV—FOLLOW UP IN PATIENTS WITH THREATENED, PREVIOUS SPONTANEOUS, OR HABITUAL ABORTIONS

Group	Abortions in treated group			Abortions in untreated group			Control rate
	Total number	Number	Percentage	Total number	Number	Percentage	
Threatened abortion	20	19*	95	20	20	100	
Previous spontaneous abortion				23	23	100	
Habitual abortion				8	8	100	
Total	20	19	95	51	51	100	75

\*1 hydrochloric acid

Moreover manganese plays a part in the maintenance of normal gestation according to Everson and Daniels, who found that stillbirths increased in mice when this mineral was omitted from the diet. Iron has been used in the form of perchloride in the treatment of recurrent abortion, according to Malpas. Simmonds has called attention to the relation of vitamin E to iron metabolism. While no tests for vitamin E were employed, it was assumed that when the prothrombin and vitamin A values were low a deficiency of vitamin E probably also existed, since it is also a fat soluble vitamin. Therefore, vitamin E in the form of alphatocopherol (Squibb) was given intramuscularly 240 milligrams monthly to some of the patients, while others received wheat germ oil, or tocopherol (Squibb) orally. It seems more than probable that there is an interrelationship of many minerals and vitamins for the maintenance of nutrition, as is well illustrated by the relation of calcium and vitamin D.

Hormonal therapy was incorporated into the regimen as indicated. The dosage of progesterone was 2 milligram weekly in the first weeks of pregnancy or when abortion threatened. A few patients received no progesterone. Some of the patients had a low basal metabolic rate, and these women were placed on thyroid extract, .015 gram 3 times daily. This medication is seldom con-

tinued beyond the fifth month when the metabolic rate begins to increase normally.

Constipation is undesirable. Mineral oil and olive oil were interdicted because their use has been found to be associated with hypoprothrombinemia in a large number of patients. Saline cathartics or enemas are preferred.

A defect in the zygote has been found by Irving and Streeter to be the cause for abortion. Since patients with repeated abortions often present a sterility problem, it may be assumed that in many instances the ova and sperms are normal. Several husbands had normal semen specimens. In the cases of women with threatened abortion, Kots and his co-workers found that only 4.9 per cent of the infants carried to viability had congenital abnormalities. In our own clinic 2.5 per cent of 27,000 infants delivered had some abnormality including extra digits, birth marks, undescended testicles, umbilical hernia, spina bifida, and hydrocephalus. It would appear to our experience to date indicates that infants born to mothers with threatened or repeated abortion are not necessarily malformed, although the tendency may be greater.

The results of the nutritional regimen in the treatment of threatened, spontaneous, and habitual abortion, as here outlined, are shown in Tables IV and V. The percentage of abortions in the threatened group is 20 per cent and it is considerably lower in the control group. No abortions occurred in the group of women with previous abortions even though one could expect that 2 and 38 per cent respectively would abort, according to Malpas. The incidence in the habitual abortion group was only 7 per cent which is much lower than the incidence of 73 to 94 per cent reported by Malpas. The total incidence of abortion in the 3 groups of patients is also decidedly lower than the incidence of 100 per cent in each of the untreated control groups.

The percentage of live births in the threatened abortion group is 100 per cent whereas rather

TABLE V—LIVE BIRTHS IN TREATED PATIENTS WITH THREATENED, PREVIOUS SPONTANEOUS, OR HABITUAL ABORTIONS

Group	Number who received cases	Live births		Under-treated
		Number	Per cent	
Threatened abortion			100	
Previous spontaneous abortion			100	
Habitual abortion	20		95	
Total	25	24	96	

\*hydrochloric acid



10. More investigation is necessary before one can state which vitamin, hormone, or mineral is solely responsible. However the treatment of choice seems to be a combination of these factors beginning before conception and continuing during pregnancy.

## REFERENCES

1. ABE, A. F., FARMER, C. J. and EMMETT, I. M. J. *Pediat.*, 8, *Lowb.*, 1936, 8.
2. BARKER, G. and GLICK, D. J. *Biol. Chem.*, 1936, 27.
3. BRAESTRUP, P. W. J. *Nutrit.*, 1936, 6, 261.
4. DANIELS, A. and EVERSON, G. J. *N. Oth.*, 1935, 9.
5. EMMETT, J. TUDALL, F. and SCOTT, W. J. *Nutrit.*, 1935, 23, 55.
6. EVANS, H. M. J. *Am. M. Ass.*, 1934, 90, 459.
7. GILMAN, J. and STERN, H. B. *Surg. Gyn. Obst.*, 1934, 72, 29.
8. IRVING, F. C. *Med. Rec.*, 1934.
9. ISRAEL, S. L., and MCKENNA, D. R. *Endocrinology*, 1934, 29.
10. J. VICK, C. T. *Med. Ch. N. America*, 1934, 31, 7.
11. *Idem*. *Am. J. Obst.*, 1930, 20, 433.
12. JAVERT, C. T. and MACK, C. *Am. J. Obst.*, 1934, 4, 400.
13. *Idem*. *Am. J. Obst.*, 1934, 43, 45.
14. KOTZ, J. PARKER, E., and KAUTZ, V. M. J. *Chm. Endocr.*, 1934, 8, 58.
15. LEVINE, P. et al. *Am. J. Obst.*, 1934, 41, 213.
16. LEE, L. *Metch. med. Wch.*, 1933, 24, 1214.
17. MACGREGOR and STEWART. J. *Obst. Gyn. Brit. Fa.*, 1930, 26, 377.
18. MALPAS, P. J. *Obst. Gyn. Brit. Empire*, 1933, 41, 437.
19. MISKOVIC, J. and DECLARTE, Y. *Zachr. physiol. Chem.*, 1936, 28, 208.
20. MONTAGNA, R., and BUTLER, A. J. *Biol. Chem.*, 1936, 127.
21. MOORE, R. A. BITTIGER, I. MILLER, M. L., and HILLMAN, L. M. *Am. J. Obst.*, 1934, 41, 107.
22. RUTHERFORD, R. N. *Surg. Gyn. Obst.*, 1934, 7.
23. SUDOVSKY, A., and WEINSTEIN, Z. J. *Lab. Clin. L.*, 1930-40, 5, 20.
24. SANFORD, H. V. SENGELSKY, I. and CHUTE, J. M. J. *Am. M. Ass.*, 1933, 13, 697.
25. EDWARDS, J. *Am. M. Ass.*, 1933, 23, 1047.
26. SENGELSKY, J. M. *Discussion of Campbell and Sengelsky*. *Am. J. Obst.*, 1930, 20, 374.
27. STREETER. Quoted by Stander, H. J. *Diagnosis (Obstetrics)*, 8th ed. New York: Appleton-Century, 1934.
28. TEEL, H., BERRY, B. and DRAPER, R. *Am. J. De. Child.*, 1932, 26, 204.
29. TOWNSEND, E. N. ROBERTS, R. C., and McFARLANE, J. A. J. *Nutrit.*, 1933, 3, 300.
30. VICK, C. T. *Metch. med. Wch.*, 1934, 24, 792.
31. WARRER, E., BRIDGEMAN, K., and SMITH, H. *Am. J. Physiol.*, 1935, 4, 667.
32. WILLIAMS, P. and F. ALBY, F. *Am. J. Obst.*, 1934, 41.

# ACUTE HEMATOGENOUS OSTEOMYELITIS JUVENALIS

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**A**LTHOUGH the incidence of acute osteomyelitis has varied little during the past few years, its surgical management has definitely changed from a radical to a more conservative regimen. This has resulted chiefly from the discovery of the sulfonamide drugs, the production of a potent high titer staphylococcal antitoxin, and the rediscovery of an old surgical principle (immobilization) concerning infected tissues. Acute osteomyelitis, regardless of its varied clinical manifestations, has always been considered a single clinical entity and treated accordingly. Consequently, the mortality and morbidity have been high and these will not be reduced until the clinical variations of this disease are appreciated. Only when we realize that acute osteomyelitis is due to the *Staphylococcus aureus* in over 83 per cent of the cases, and that not the bacteria, but their toxins are responsible for the systemic reaction and local destruction of osseous tissue, can we intelligently treat the disease and obtain complete recovery, with minimal bone destruction.

There are over 60 varieties of staphylococcus and according to Spink, no less than 8 different types of toxins are derived from these. Each type of toxin has a definite specific reaction on the tissues in which it has been generated (local reaction) as well as on the generalized somatic cells and glands (systemic reaction). These toxins, reacting in the tissues, destroy both the fixed and mobile tissue cells. The most powerful of these toxins will kill a person within 15 to 36 hours, as demonstrated in the Queensland cases. Twelve children who received diphtheria toxin succumbed within 15 to 36 hours. Deaths were due to contamination of the diphtheria culture in obtaining the toxoid from lethal toxins of the *Staphylococcus aureus*.

The necrogenic toxin and the toxin that increases diffusibility of both the bacteria and their toxins in the tissue cause extensive destruction of the osseous tissue. The hemolytic, leucocidin, and fibrinolysin toxins together with the power of diffusibility are responsible for the failure of localization of the infection. Therefore, the early high mortality in acute osteomyelitis is caused from the profound toxemia with or without bacteremia. The bacteremia in all probability is due to a bac-

terial thrombophlebitis in the osseous tissue. The number of colonies in the circulating blood is entirely dependent upon the degree and extent of the thrombophlebitis which in turn is determined by the virulence of the organism, both being secondary to the type of toxin liberated. That thrombophlebitis exists in all pyogenic infections is a well established pathological law. However, the extent and size of the veins involved are dependent upon the type of toxin liberated by the staphylococcus and vary considerably in degree. Therefore, it is readily understandable that early neutralization of the toxin not only will inhibit all the side effects of the infection, such as extensive injury to the somatic tissues including all organs and glands, but will prevent local osseous tissue destruction as well. If this can be accomplished, then the somatic tissue cells, especially the reticuloendothelial system, can destroy the bacteria both by phagocytosis and the liberation of bacteriolytic and agglutinins. The sulfonamides are a valuable adjunct because they inhibit bacterial growth and thus prevent toxin liberation.

Acute osteomyelitis can be divided into several clinical types depending entirely upon the kind of organism and its toxin. In teaching, I have classified acute osteomyelitis clinically to correspond with the pathological physiology: (1) Profound systemic effects with minimal local reaction is due to the lethal or sublethal toxin liberated by the staphylococcus. Bacteremia may or may not be present. Blood culture is, however, positive in a high percentage of these cases. (2) Profound systemic as well as local reaction is caused by liberation of the lethal or sublethal toxin and is accompanied by early cellulitis resulting in pus formation with or without associated bacteremia. (3) Minimal systemic and maximal local reaction without bacteremia is probably the result of the necrogenic toxin and the spreading factor of "Duran-Reynolds." Pus forms rather early in the majority of cases. (4) Minimal systemic and local reaction is rare and frequently leads to Brodie's abscess. Here virulence of both the staphylococcus and its toxin is of a mild character. (5) The streptococcal form, occurring in young children and babies, usually causes minimal bone destruction. (6) In the chronic forms, such as Brodie's abscess and chronic sclerosing osteomyelitis of Garre, the systemic and local reactions are nil.

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Infection within osseous tissue varies greatly depending upon the degree of bone involvement. In some, early localization occurs, whereas in others, there is present a diffuse marrow and haversian cellulitis which localizes to one area in the bone or fails to localize, resulting in a diffuse cellulitis of the entire shaft of the bone. If the infection begins near the cortex in the metaphysis and localizes early it ruptures and a subperiosteal abscess forms. If the infection begins in the metaphysis near its center close to the beginning of the bone marrow a diffuse cellulitis of the bone marrow appears. This form of infection is comparable to the cellulitis of soft tissue. In lymphangitis and cellulitis if the infection localizes, a simple abscess appears. If not, the whole cellular structure of a part becomes involved and frequently death occurs. It is this diffuse osseous and bone marrow cellulitis and lymphangitis which is responsible for the profound systemic reaction so frequently encountered in acute osteomyelitis. Therefore, the anatomical location of the primary infection within the metaphysis has a direct bearing upon the type and extent of the osseous lesion. Thus, the pathological condition of the bone can be classified as follows: (1) Diffuse cellulitis involving the entire shaft, (2) diffuse cellulitis involving the entire shaft with localization to one or more areas, resulting in multiple abscesses or a single abscess. Occasionally in this type an abscess is centrally located at each end of the shaft. (3) Superficially located primary focus with early subperiosteal rupture and abscess formation which frequently ruptures into the soft tissue. In these cases a minimal amount of bone is destroyed. (4) Primary focus located near the epiphysis in the center of the metaphysis, resulting in a centrally located abscess. Often the joints are involved in the two latter. A careful evaluation of both systemic and local reactions will indicate the pathological condition which is present and which will develop in the osseous tissue.

Based on the pathological condition, the treatment is simple and the results, in the majority of instances, will be most gratifying. Treatment consists of complete rest, early neutralization of the toxemia, early prevention of bacterial growth, maintenance of water balance, blood volume, plasma volume, blood cellular volume and blood electrolytes, complete immobilization of the involved part, daily blood cultures in all cases, maintenance of nutrition and finally operation only when cellulitis has localized with abscess formation.

Early neutralization of the toxin and prevention of bacterial growth will immediately over-

come the toxemia, thus prevent bone destruction, and probably obviate the necessity of operative in a large number of cases. This purpose can be accomplished by the daily administration of 60,000 to 100,000 units of a potent antistaphylococcal serum until toxemia subsides. The intravenous or oral administration of sulfathiazole prevents the multiplication of bacteria and, consequently, the formation of toxin by bacteriostatic action. This allows the reticuloendothelial system to manufacture bacteriolysin and agglutinins as well as phagocytes which eliminate the infection. Early immobilization will minimize and prevent the spread of infection, especially to the joints. The only other treatment is supportive, i. e., injections of glucose in Ringer's solution and plasma and whole blood transfusions. This therapy must be continued until the patient can supplement intravenous medication by ingesting the necessary food. Large doses of vitamins, especially B and C, should be given intravenously during the toxic phase and later by mouth. Vitamin C changes procollagen to collagen fibers. Vitamin B is essential for the normal function of the nervous system and should be given in 10 to 30 milligram doses. Vitamin D and calcium should be given after the toxemia subsides.

Frequent radiographic studies and needling for pus after the toxic stage should not be forgotten. If the roentgenograms demonstrate bone necrosis and the temperature returns to normal, operation should be deferred and frequently will not be necessary. However if pus is obtained, operation under local anesthesia is indicated. If there has been local central bone destruction and the toxemia has subsided but the patient continues to have fever, operation is indicated if it is cautiously undertaken. If the patient can be treated within 24 hours of onset of the disease according to this plan, bone destruction will be minimal.

Any surgical procedure undertaken during the acute stage will result in a high mortality and morbidity with serious disability. Although operation is contraindicated in the majority of other infections with profound toxemia and bacteremia, some surgeons insist on using the drill and chisel in similar cases of osteomyelitis. Boster reported 3 cases of acute osteomyelitis with a positive blood culture in which early operation was performed with a mortality of 50 per cent, whereas in 2 cases with negative blood cultures, early operation resulted in only a 1 per cent mortality. Neither staphylococcal antitoxin nor sulfonamides were used. These statistics emphasize the importance of instituting proper treatment early in acute hematogenous osteomyelitis.

# EDITORIALS

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## MODERN METHODS IN ANESTHESIA AND THE WAR

LACK of experience of a situation sometimes leads to ill founded conclusions. It is probable that neither the care of accidents in civil practice nor the performance of necessary surgical procedures for soldiers and sailors in time of peace have constituted an adequate background of experience from which to predetermine our conduct under the circumstances of war. Doubtless both surgeon and anesthetist will modify their plans of action as experience with battle casualties becomes extensive in the months and years to come. It would seem advisable, therefore, to emphasize principles rather than minutiae of practice in our preparation for the duties which confront us.

There is a variety of anesthetic agents available for the relief of pain. Several techniques for the administration of these drugs have been used in civil practice. On superficial consideration, it might be concluded in the interest of simplicity that one or two drugs

given by one or two techniques should be chosen for military practice. However, further reflection brings out many objections to such a conclusion. For instance, it may be assumed that the variety and gravity of disturbances of the physiological functions of the respiratory and circulatory systems which are encountered among the wounded will be as great as, if not greater than, the variety of such disturbances common in civil practice. Hence, the demand for a varied attack by the military anesthetist may be even greater than in civil practice. A physician trained in anesthesiology may contribute many services in addition to the prevention of pain due to operations. The management of fluid depletion, transfusion and other intravenous therapy, inhalation therapy, the maintenance of free breathing under all circumstances, the use of manual and mechanical aids to respiratory exchange and the judicious relief of pain before and after operation or for nonsurgical cases are some of the fields in which comprehensive knowledge and experience in anesthesiology may be helpful. Emphasis upon principles and a broad consideration of techniques in our preparation for war has therefore seemed wise. The Offices of the Surgeons General have very laudably instituted certain changes of a promising nature. Whether or not Tables of Organization have yet been revised to recognize fully the needs of anesthesiology, there has been an encouraging assignment of qualified anesthetists to each hospital if not to each surgical team. Medical officers on active duty are being instructed in anesthesiology in civilian as well as military hospitals.

As the number of anesthetists available in the medical corps increases, the care with



which they are assigned to duty becomes important. The director of anesthesia in a large hospital ought to be an officer with broad experience in a similar position in civil life. If the scarcity of men with such experience makes it necessary to assign officers trained during the present emergency to positions of such responsibility due consideration ought to be given to previous executive experience in other fields. As soon as the number of well qualified officers is sufficient it should be recognized that one anesthetist may be assigned with advantage to every surgical team. Particularly is this true of units dealing with chest and abdominal wounds. How extensively technician aids (hospital corps men or nurses) can be utilized safely will depend upon the caliber of instruction and supervision which the officer in charge of anesthesia is capable of giving.

The type of apparatus provided for the anesthetist in our armed forces is of some importance. The proper tools of any "trade" come into existence in response to evident need as a result of long experience. It is obvious that present lists in tables of supplies of the military organizations have had to be made up without observation of the needs, and with very little experience in anesthesia under war conditions. An honest effort to provide the best equipment on the market has evidently been made. Certainly no expense has been spared. News from anesthetists in active service indicates that certain of the simpler but more essential and less expensive pieces of equipment are not available. For instance, a simple assembly of a face mask, strong rubber breathing bag and proper artificial airways with or even without a cylinder of oxygen constitutes a very efficient aid for resuscitation. With these articles available, respiratory obstruction, depression or arrest may be quickly and satisfactorily treated. In

addition a simple folding type of anesthetic laryngoscope with two or three artificial breathing tubes, and a small suction catheter to pass through such tubes into the bronchi, puts the officer in command of the situation even when the lower respiratory tract is contaminated by blood or other fluid. If a properly shaped canister of soda lime granules is available to insert between the mask and breathing bag mentioned as useful for artificial respiration an efficient apparatus is provided for the administration of ether (or the gaseous agents). A small supply of oxygen is necessary under such circumstances. Thus equipped an officer familiar with modern practice in anesthesia can administer atmospheres under positive pressure a procedure sometimes helpful in the treatment of chest injuries, and for anesthesia during operations within the chest. The bulk, cost and efficiency of simple equipment of the sort just mentioned would seem particularly well adapted to military needs. By competent officers, it might even be used under field conditions.

Medical officers, whether serving on land or sea, not infrequently find themselves under the necessity of being "all things to all men." Knowledge or skill in only one specialty cannot avail at such times. Common sense is the best substitute for deficiency of either knowledge or skill. It must be admitted, however, that among the more frequent disabilities encountered will be acute interference with the normal functions of respiration and circulation. Major injuries to the upper and lower respiratory tract, loss of blood and severe pain are common results of battle. The anesthetized patient during operation provides ideal material with which the teacher can demonstrate and the officer may practice the care of respiratory and circulatory emergencies. Protection of respiratory and circula-

tory function is the essence of good anesthesia. The "bad results" of anesthesia are, in no small measure, due to neglect of such protection. It seems obvious, therefore, that knowledge of anesthesiology, skill in the replacement of fluids, in the insertion of artificial airways, in safe and efficient methods of artificial respiration, in clearing the respiratory tract of blood or fluid, together with skill in relieving pain will be found useful wherever the medical officer's duties may take him. The courses in anesthesiology sponsored by the War Department are designed to provide instruction along these lines.

Fear has been expressed that short term instruction in the surgical specialties now sponsored by the War Department may result in a surplus of poorly trained specialists coming

back to civilian practice after the war. Such a condition is not likely to arise in the field of anesthesiology. It is important to remember the definite shortage of clinical anesthetists which existed prior to this war. Those officers receiving instruction and experience during the war will be in a position to render better service than formerly to their patients when they return to civil practice, regardless of whether or not they choose anesthesia as their special field.

The Surgeons General of the Army and of the Navy are to be congratulated upon their efforts to provide modern anesthesia, as well as modern medical service of every sort, to the armed forces. It seems probable that the results will justify this attitude.

RALPH M. WATERS

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

In any small book as *Acute Injuries of the Head* by Rowbotham (187 pages) the author invariably faces a serious criticism when he attempts to cover such a large subject as acute injuries of the head in such limited space. He runs the risk of being accused of knowing or of believing and practicing no more than he has actually written, though obviously in most cases this fact must not be true. As he indicates in his preface, Rowbotham is aware of this possibility.

In order to cover the subject completely the author has not deviated from his outline of discussion; the book is absolutely lacking in any discussion or padding. In fact, this is so much true that one frequently finds broad and arbitrary statements which need explanation and elaboration. The treatment of diagnostic signs and symptoms is clear and concise, with sufficient detail, and the short descriptions of the gross brain pathology are excellent. The author's use of drugs in the treatment of acute cerebral injury will be questioned by many surgeons, but no one will take objection to his views on the importance of local anesthesia in this type of surgery. On page 81 the statements referable to the use of mannitolic mannureline in the repair of cerebral trauma should never be found in a text printed as late as the spring of 1942. The author seems to find indications for operation in cut cerebral trauma much more frequently

than does the average American neurological surgeon, and he has stated clearly his indications for subtemporal decompression when intracranial tension is greatly increased due to swelling of the brain. Such an operation is indicated when there is (1) retrogression following a period of improvement which cannot be controlled by spinal drainage or by intravenous hydration (2) a delayed decerebrate rigidity (3) fixed dilated pupil or (4) profound unconsciousness associated with persistently high cerebrospinal fluid pressure. The uninitiated would not learn from the discussion on the operative treatment of increased intracranial tension and cerebral herniations just what insurmountable difficulties and real trouble can be created by surgery of such nature.

There is a brief but useful and unconventional discussion of the posttraumatic syndrome and some useful notes on the medicolegal aspects of craniocerebral injuries and surgery. The illustrations, though plentiful, serve their purpose splendidly. The greatest criticism of the book lies in some of the dogmatic principles of treatment, especially those relative to surgical treatment, and though such methods may doubt have served well in the hands of Rowbotham, by no means are most such principles in common use in America. Appearing at this time when the cerebral injuries of warfare are increasing steadily it is most interesting, 6 years or so hence, to recall this pathy book in the light of our then newly acquired experience.

JOHN MURPHY

*Acute Injuries of the Head, Trauma (Diagrammatic), Traumatic Complications, 4th Edition.* By O. F. Rowbotham, B.Sc. (M.B., Ch.B., F.R.C.S. (Eng.)), with a foreword by Norman M. Sweet, M.B., Ch.B. (Ed.), F.R.C.S. (Ed.). Baltimore: The Williams & Wilkins Co. 1942.

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

*SAFE DELIVERANCE.* By Frederick C. Irving, M.D. Boston: Houghton Mifflin Co., 1941.

*A CADEIRA OBITEREA DO PARRICIDIO DO PRESENTE.* By Costa Saavedra and A. Saavedra. Oporto, Portugal: Typo e Sobrelito, 1942.

*ADVERTISING IN BLOOD TRANSMISSION.* By Benjamin M. Bernheim. New York: Smith & Dorrell, Inc., 1942.

*CANCER OF THE UTERUS.* By Elizabeth M. Gordon, C.B.E., M.D. London: Oxford University Press, 1942.

*PUBLIC HEALTH AND PREVENTIVE MEDICINE.* By Mor-

ris C. Kahn, M.A., Ph.D., D.Sc., Yale and London, New York, and Toronto: Oxford University Press, 1942.

*ONCOLOGICAL SURGERY.* Morris A. Goldberger, M.D. F.A.C.S. London, New York, and Toronto: Oxford University Press, 1942.

*DISEASES OF THE GASTRO-INTESTINAL TRACT.* By Walter Winkler, M.D., B.S. London, New York, and Toronto: Oxford University Press, 1942.

*ONCOLOGY.* By William H. Mescher, A.B., M.D. F.A.C.S. London, New York, and Toronto: Oxford University Press, 1942.

*THE HEMORRHOID DISEASE AND THE PREVENTION OF HEMORRHOIDS.* By Arnold J. Quirk, Ph.D., M.D. Fort Belld, Ill. and Baltimore: Sid Charles C. Thomas, 1942.





Portrait by Eugene Spaulding

## GEORGE CRILE

NOVEMBER 1 1864—JANUARY 7 1943

# SURGERY

## GYNECOLOGY AND OBSTETRICS

*An International Magazine, Published Monthly*

VOLUME 76

FEBRUARY, 1943

NUMBER 2

### CORRELATION OF GASTROSCOPIC AND PATHOLOGICAL FINDINGS IN GASTRITIS

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ACCURATE data correlating what is seen by the gastroscopist in the living stomach with what is seen by the pathologist in the dead stomach are hard to obtain and often difficult to evaluate. An area may be described gastroscopically as reddened, hemorrhagic, eroded, verrucous, etc., and at least nine times out of ten no pathological check is possible for usually patients with gastritis alone do not come to autopsy and do not require operation. If, by chance, such a patient does come to autopsy the objection may be raised that autodigestion has rendered almost valueless any gross or histological study of the gastric mucosa. In surgically resected specimens operative trauma from handling or clamping the stomach has been said by Schindler, Necheles, and Gold to invalidate the findings. Faber's monograph on gastritis is a real contribution to our knowledge of the subject but the work is purely from the pathological standpoint as no gastroscopic observations were made. Swalm and Morrison examined 25 cases with the flexible gastroscope shortly after which biopsies were obtained by Dr. Chevalier L. Jackson and his associates, through the open tube gastroscope. These writers conclude that

From the Massachusetts General Hospital

histological diagnosis agrees with gastroscopic diagnosis in normal or gastritis stomachs in 52 per cent of cases and that the gastroscopic appearance of a severe gastritis is usually verified by the histological examination but the gastroscopic appearance of a mild or moderate degree of gastritis or normal stomach may be contradicted upon histological examination. While this series of cases was apparently studied with care and without prejudice, the number of cases examined was small and the histological verification of gastroscopic observations disappointing.

This report is based on a careful analysis of 51 selected cases in which satisfactory gastroscopic study was followed by histological examination. Eighty-four cases were discarded as unsatisfactory because of incomplete gastroscopic notes, poor microscopic sections, small biopsy specimens only, or too long a time interval between gastroscopy and operation. Six biopsy cases were discarded because we felt it was not fair to either the gastroscopist or the pathologist to expect the latter to make a diagnosis as to the entire gastric mucosa from a small and sometimes mutilated biopsy specimen. In this series of 51 cases there were 23 ulcers (18 gastric, 3 duodenal, 2 jejunal), 22 carcinomas, 2 cases of

gastritis alone 2 lymphomata, 1 benign polyp and 1 normal stomach. Specimens were obtained in all cases by surgical resection.

A control series of 50 stomachs removed at autopsy as shortly as possible post mortem (2 to 3 hours on the average) and fixed with particular care was utilized for purposes of comparison. The detailed histological studies of the two series will be presented elsewhere. They were carried out with two purposes in mind. First, it seemed important to check upon the possibility raised by the reports of Schindler Necheles and Gold that important inflammatory changes may develop in the course of surgical resection due to the continued action of gastric juice upon a mucosa deprived of its blood supply by the surgeon's clamps. We found few mucosal defects such as these authors illustrate in our material provided (1) the resection was performed by a competent surgeon (2) the specimen was promptly delivered to the pathologist without palpation by numerous intervening hands, and (3) the organ was fixed immediately after it was opened to prevent drying of the surface. When found, such lesions were dismissed as artefacts. The slight plasma cell infiltration illustrated by these authors as evidence of inflammatory reaction about the mucosal defects is unconvincing. Considerable local variation in the almost invariable plasma cell infiltration of the gastric mucosa is the rule and of all possible types of wandering cell infiltration which might be attracted to such an acute lesion the plasma cell the prototype of chronic inflammatory processes, is the least likely to make such an immediate response.

We found only two fairly constant variations between the resected specimens and comparable cases from the autopsy group other than the more perfect fixation of the former. The tips of the villi were more frequently edematous in the resected group and the loose layer of fibrous tissue between the muscularis mucosae and the main muscular layer was regularly wider. Capillary engorgement, degrees of neutrophilic leucocyte infiltration, frequency of erosions and of interstitial hemorrhages were not disproportionate in similar cases from either group. Consequently we believe that resected specimens,

despite a slight tendency to edematous swelling are entirely suitable for comparative study of histological and gastroscopic findings the primary purpose of this report.

The second necessity for a control group was to study the chronic inflammatory infiltration of plasma cells, lymphocytes, and eosinophiles which virtually every stomach shows in varying degree. For purposes of rough quantitation four grades were distinguished. Grade I was defined as scattered small foci of plasma cells, grade II as a narrow continuous band localized sharply about the neck zone of the glands. In grade III the band has become wider and may occupy one-third to one half of the total width of the mucosa. Grade IV extends from this to complete infiltration of the mucosa from villi up to muscularis mucosae. It should be pointed out that this division is entirely artificial and simple for purposes of convenience since every grade of transition from the least to the maximal can be observed. It is, furthermore important to emphasize that the differences are purely quantitative not qualitative and maximal infiltration of grade IV represents merely an exaggeration of a process to be found in virtually every stomach.

The results of quantitative estimation of the degree of infiltration of the nonacid producing and the acid producing (labelled respectively for the sake of brevity antrum and fundus) mucosae of the control series and the resected specimens appear in Table I. The figures indicate the percentage of specimens examined showing the various grades of infiltration.

TABLE I—CHRONIC INFILTRATION

Grade	Autopsy series			
	I	II	III	IV
Antrum	8	4	45	45
Fundus	4	30	35	31
Grade	Resected specimens			
	I	II	III	IV
Antrum		3	26	71
Fundus		4	30	66

From inspection of these figures it is evident that no stomach was found without some infiltration of at least the antral portion (including 1 infant 36 hours after birth) and that grades I and II (Figs. 1-2) of infiltration are so frequent

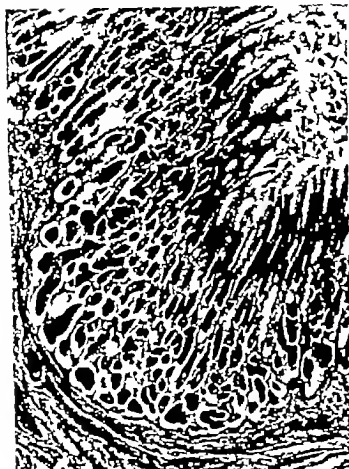


Fig 1



Fig 2

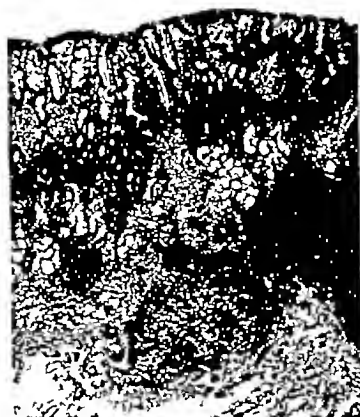


Fig 3

Fig 1 Photomicrograph showing Grade II chronic infiltration of the fundus limited to the neck zone within normal limits  $\times 30$

Fig 2 Neck zone from antral region showing plasma

cell infiltration and physiological exudate of leucocytes into the gland  $\times 170$

Fig 3 Grade IV, antrum Pathological exaggeration of chronic infiltrate occupying two-thirds of mucosa  $\times 30$

that they must be considered to be within normal limits Grade IV (Fig 3), which was rarely found in the control series but was common in the diseased stomachs of the resection group, is obviously pathological Grade III (Fig 4) is on the border line Infiltration of this intensity in the fundus is probably abnormal and was so classified in this study

In the antrum, where the degree of infiltration tends to run one grade higher than in the fundus we chose to consider grade III within normal limits and only grade IV as definitely pathological In the comparisons with the gastroscopic findings to be detailed below it has been assumed that chronic infiltrates of grade IV intensity in the nonacid producing



Fig 4

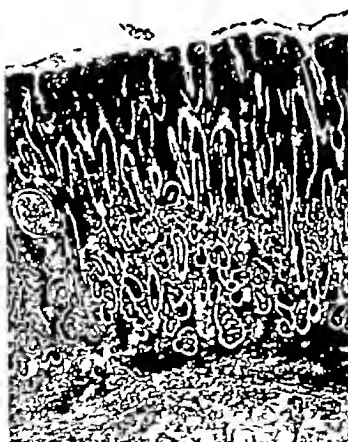


Fig 5



Fig 6

Fig 4 Grade III, antrum Upper border of normal limits of infiltration. Classified as normal  $\times 30$

Fig 5 Acute or superficial gastritis Mucin vacuolization gone and leucocytes fill upper third of mucosa.  $\times 30$

Fig 6 Higher power of portion of Fig 5 The epithelial cells have lost all functional differentiation and large numbers of leucocytes are present beneath and between them  $\times 170$





Fig. 7

Fig. 7. Early atrophy of the fundus. Shortening of the glands with partial loss of differentiation.  $\times 30$



Fig. 8

Fig. 8. Atrophy of antrum. Few recognizable gastric elements remain. Intestinal metaplasia is almost complete.  $\times 30$

mucosa and of grades III and IV in the acid producing mucosa are the histological counterparts of so called hypertrophic gastritis. If as we believe we have demonstrated this is the case hypertrophic gastritis represents an exaggeration of the 'physiologic gastritis' of normal stomachs.

A second type of gastritis, to be correlated below with the "superficial gastritis" of the gastroscopist, presents significantly different histological findings. In the chronic type which has been described the differentiation and apparent functional integrity of the epithelial elements of the mucosa is remarkably well maintained in even the most severe grades. In this second type the mucin vacuoles which normally almost fill every cell above the neck zone of the glands including all the surface cells covering the apices of the villi become smaller and smaller until in the severe grades they disappear entirely (Fig. 5). Along with this gradual diminution in the mucous vacuolization polymorphonuclears appear in large numbers in the interstitial tissues of the upper portions of the mucosa. Frequently they can be found in large numbers just beneath the surface epithelium and wandering between these cells into the lumen of the stomach (Fig. 6). In severe cases the failure of differentiation of the epithelial cells may extend downward from the neck zone toward the bases of the glands and in such instances leucocytes will be found as deep as the muscularis mucosae. Superficial gas-

tritis, then is superficial in the sense that the surface is always involved but not in the sense that only the upper portion of the mucosa is abnormal. It is an acute exudative process and as such can be superimposed on either of the other two types.

A word of caution must be inserted regarding the significance of neutrophilic leucocytes in the mucosa. Hamperl has clearly shown that neutrophils may frequently be found in normal stomachs but he also clearly pointed out that they like the early stages of plasma cell infiltration, are sharply limited to the neck zone. The leucocytes must stray widely from this area and be associated with some deficiency of mucous vacuolization before the diagnosis of acute exudative or in gastroscopic terms, superficial gastritis is justified.

The third clearly characterized type of gastritis is the atrophic. In the atrophic mucosa the significant feature is the progressive diminution of the epithelial elements, particularly the differentiated elements at the bases of the glands (Fig. 7). The glands become shorter they lose their terminal convolutions a gap appears between the base of the glands and the muscularis mucosae. Gradually they become more widely spaced and the intervening interstitial tissues show proportionate increase. Usually the muscularis mucosae is infiltrated with fibrous tissue and the layer of underlying loose areolar tissue often becomes narrowed and fibrous. This process may be accompanied by

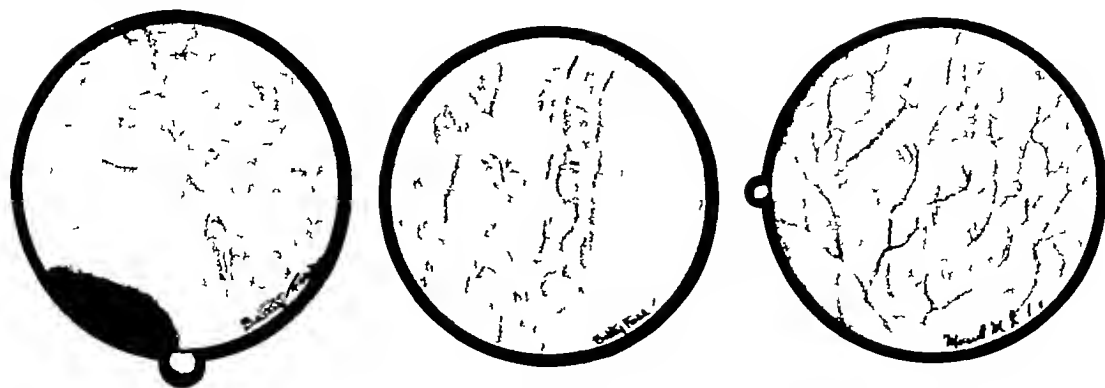


Fig 9 Hypertrophic gastritis with erosions Fig 10 Superficial gastritis

Fig 11 Atrophic gastritis

any grade of acute or chronic inflammatory infiltration. Metaplasia of the intestinal type appears in more and more numerous foci and eventually may entirely replace all proper gastric elements (Fig 8).

By gastroscopy we describe three types of gastritis: hypertrophic, superficial, and atrophic. Not infrequently in the same stomach there will occur a mixture of two types, superficial and atrophic or superficial and hypertrophic. In one instance gastroscopy showed marked hypertrophic gastritis, moderate superficial gastritis and one area of localized atrophy. This case was corroborated by the pathologist in all respects.

By hypertrophic gastritis (Fig 9) the gastroscopist means a mucosa studded with verrucous elevations having a dull surface with few highlights and sometimes a beaded appearance to the rugae. The pathologist does not see verrucous elevations in the mucosa to which he can certainly attribute pathological significance. This, however, does not disprove their existence in the living stomach nor does it prove their insignificance in gastroscopic diagnosis. The counterpart of the hypertrophic gastritis described by the gastroscopist appears to be the chronic gastritis which the pathologist recognizes by an exaggeration of the zone of plasma cell infiltration which in some degree is found in almost every stomach.

By superficial gastritis (Fig 10) the gastroscopist means increased reddening, edema, and adherent secretion. This type we have found to correspond with the acute exudative

gastritis described by the pathologist. Superficial gastritis may, therefore, be regarded as an acute process and may be superimposed on the atrophic or hypertrophic varieties.

The gastroscopist and pathologist agree in defining atrophic gastritis (Fig 11) as atrophy of large areas of the mucous membrane, seen gastroscopically as a pale, thin mucosa with a network of easily visible blood vessels. Whether or not atrophic gastritis is the end-stage of an inflammatory process and, therefore, a true gastritis, or the result of a vitamin or other deficiency and, therefore, better termed a gastric atrophy, is an unsettled problem beyond the scope of this paper. There is some evidence that both an inflammatory process and a deficiency factor may play a part.

In comparing the gastroscopic and pathological findings in all types of gastritis in this series one finds complete correlation in 28 of 51 cases (54.9 per cent), partial correlation in 17 (33.3 per cent), no correlation in 6 (11.8 per cent). There was, therefore, complete or partial correlation in 45 cases (88.2 per cent). By partial correlation we mean that the pathologist has confirmed one part of the gastroscopist's observations but has not confirmed another part or has added an observation not mentioned by the gastroscopist. For example, in one case (U#-44513) the gastroscopist noted multiple benign gastric ulcers with erosions and superficial gastritis. The pathologist noted extensive and severe gastritis with focal atrophy of significant dimensions.

but minimal intestinal metaplasia. Since no atrophy was noted by the gastroscopist this case is classified as only partial correlation. The 6 cases of complete disagreement were as follows:

R. H., UF-333 81, male aged 7 years. Resection for gastric ulcer. The gastroscopist reported definite atrophy of the anterior wall. The pathologist found severe antral and moderate fundic gastritis but no atrophy. The disagreement here is complete and cannot be satisfactorily explained. Possibly the supposed atrophy seen at gastroscopy was due to overinflation of the stomach with air although this is a mistake which should rarely occur or perhaps the pathologist had no section from the localized atrophic area of the anterior wall. A gastroscopic not was made as to the condition of the mucosa near the ulcer which was partly obscured by mucus and debris.

G. W. F. UF-3905, male aged 47 years. Resection for peptic ulcer. The gastroscopist described reddening and edema of the antrum proximal to the ulcer. The pathologist reported infiltration of the antrum but no more than was found in series of control stomachs.

M. J. UF-343184, female, aged 66 years. Gastric resection for gastric ulcer. Gastroscopy showed normal appearing mucosa. Histological examination of specimen resected days later as reported as showing extremely severe cut diffuse antral and fundic gastritis. This case represents complete failure of the gastroscopist due either to insufficient attention to the mucosa (the main problem being the ulcer) or to failure of the gastroscopic method to detect gastritis in this case. Since the pathologist reported an extremely acute process, it is possible although unlikely that some of the acute gastritis developed in the day interval between gastroscopy and operation.

J. S., UF-83404, male aged 4 years. Resection for pyloric ulcer. Gastroscopy revealed no evidence of gastritis. The resected specimen 3 weeks later however showed very severe trophic gastritis. This discrepancy is probably due either to poor observation by the gastroscopist or failure of the gastroscopic method. We believe the 3 weeks time interval is much too short for the development of severe atrophy.

E. M. P. UF-0833, male aged 6 years. Resection for carcinoma. Gastroscopy showed marked superficial gastritis. The resected specimen 6 days later showed no more than the usual infiltration seen in the control group.

E. S., UF-186799, male, aged 70 years. Resection for carcinoma. Gastroscopy showed slight superficial gastritis but examination of the resected specimen revealed moderate atrophy. It is hardly likely that slight superficial gastritis would mask moderate atrophy. Therefore this case is recorded as complete failure in correlation.

Summarizing these 6 cases of complete disagreement we find the following possible explanations: (1) localized area of stomach described by the gastroscopist not sectioned by the pathologist (2) mucus and debris obscuring gastroscopist a view and warping his judgment, (3) changes in the mucosa due to time interval (even a few days will alter the acute picture) (4) poor gastroscopic view of the antrum in some cases, bearing in mind that the pathologist often finds the most marked gastritis in the antrum, (5) overinflation of the stomach with air stimulating atrophy. We do not feel that lack of correlation in 6 cases is any cause for concern. In fact, we believe that the complete and partial correlation in 45 of 51 cases is excellent corroboration of the gastroscopic method of diagnosis in gastritis.

Analysis of each of the three gastritis groups separately reveals further interesting data. Sixteen cases showed hypertrophic gastritis by both methods and 22 cases showed no hypertrophic gastritis by either method or a total of 38 cases with complete agreement (74.3 per cent). In the 13 remaining cases (35.5 per cent) gastroscopy showed hypertrophic gastritis not corroborated by histology in 4 and histological examination disclosed a chronic gastritis which had not been observed by gastroscopy in 9. Here again the explanation for this discrepancy seems to lie at least partly in the fact that in 6 of the latter 9 cases the gastritis described by the pathologist was confined to the antrum, a percentage error of 12. The time interval should be of comparatively little significance in this group but a superimposed acute superficial gastritis might mask for the gastroscopist an underlying chronic hypertrophic gastritis.

Twenty five cases showed superficial gastritis both gastroscopically and histologically and 9 cases showed no superficial gastritis by either examination. In other words, there was complete agreement as to the presence or absence of superficial gastritis in 34 cases (66.7 per cent). There was lack of correlation on this point in 17 cases (33.3 per cent), in 8 of which gastroscopy showed superficial gastritis not confirmed by histology and in 9 of which histological examination disclosed some acute

gastritis which had not been observed by gastroscopic examination. Since, as aforesaid, superficial gastritis as described by the gastroscopist is probably an acute process corresponding to acute exudative gastritis as seen by the pathologist the time interval between gastroscopy and operation would be of great importance and even a few days delay might account for great discrepancy. Another factor of significance is the fact that the pathologist frequently finds the process localized to the antrum, an area sometimes relatively poorly seen by the gastroscopist. In this group the error possibly attributable to this source would be 8 per cent.

The cases showing atrophic gastritis were also analyzed separately. In this group 4 cases showed atrophy by both methods of examination and 30 cases showed no atrophy by either method or a total of 34 cases with complete correlation (66.7 per cent). In the remaining 17 cases (33.3 per cent) gastroscopy showed atrophy not confirmed by histology in 1 and histological examination disclosed atrophy not observed by gastroscopic examination in 16. The explanation for this discrepancy would again appear to lie partly in the fact that in 11 of these cases the atrophy was confined to the antrum, the area which as has already been noted is sometimes poorly visualized by gastroscopy. In this group the error possibly ascribable to this cause would be 22 per cent. In some cases the atrophy may have been masked gastroscopically by a superimposed superficial gastritis.

#### CONCLUSIONS

This report is based on a comparative gastroscopic and histological study of 51 cases selected from a total of 135 on the basis of completeness of gastroscopic notes and adequacy of histological material. All were surgically resected specimens.

We believe that surgically resected stomachs are satisfactory for the pathological

study of gastritis and that the element of trauma incident to surgical procedure can be readily distinguished histologically from real gastritis.

We believe that biopsy specimens are inadequate for satisfactory gastroscopic-pathological correlation not only because they afford such a limited section of gastric mucosa for histological study but also because they are more likely to be badly traumatized than are surgically resected specimens.

Superficial gastritis as described by the gastroscopist corresponds to the acute exudative gastritis of the pathologist. The term atrophic gastritis is used by both gastroscopist and pathologist to denote the same type of mucosa. Hypertrophic gastritis as described gastroscopically corresponds to an exaggerated form of the physiological plasma cell and lymphocytic infiltration of the normal stomach.

In the 51 cases in this series including all types of gastritis there was complete gastroscopic-pathological agreement in 28 cases (54.9 per cent) and partial agreement in 17 cases (33.3 per cent) or a total complete or partial agreement of 88.2 per cent. There appeared to be no correlation in the 6 remaining cases (11.8 per cent).

Analysis of the separate types of gastritis showed agreement in 74.5 per cent of the hypertrophic, 66.7 per cent of the superficial and 66.7 per cent of the atrophic.

We believe that the agreement in this series has been very good and conclude that such close pathological verification of the gastroscopic findings in gastritis is an important indication of the value of gastroscopy.

#### REFERENCES

1. IABER, K. *Gastritis and its Consequences*. New York: Oxford University Press, 1935.
2. HAMPERL, H. *Beitr. path. Anat.*, 1932, 90: 85-141.
3. SCHINDLER, R., NICHILIS, H., and GOLD, R. L. *Surg. Gyn. Obst.*, 1939, 69: 281-286.
4. SWAN, W. A. and MORRISON, L. M. *Am. J. Digest. Dis.*, 1941, 8: 391-397.

## A METHOD OF COLECTOMY FOR DESPERATE CASES OF ULCERATIVE COLITIS

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**P**ATIENTS suffering from severe ulcerative colitis not infrequently appeal for surgical aid after they have exhausted all medical treatment and when therefore they are in a late stage of the disease and suffering from profound anemia the result of repeated bleedings and from great emaciation and debility caused by toxic absorption from the extensive ulceration. No half measures, such as appendicostomy, cecostomy, or even enterostomy, are of any permanent avail in these patients. Nothing short of colectomy will save such a patient's life. But in circumstances such as these a colectomy as usually performed, would assuredly fail because the patient's general condition would not permit such a big operation and even if it did the tissues of the intestinal wall would be so deficient in vitality that no union would take place in any intestinal anastomosis. How a colectomy (practically total) in a patient almost moribund as a result of ulcerative colitis, can be carried out by the exercise of patience and by the contrivance of a "sliding scale" type of operation, is illustrated in the interesting record of the following case.

A female patient aged 41 years (M.L.), had been ill for period of 6 months, during which she suffered from a progressive deterioration of her general health, severe secondary anemia which did not respond to treatment and prolonged attacks of severe diarrhea.

A 3 day attack of acute diarrhea associated with some ill localized abdominal pain and tenderness led to an emergency operation on the belief that she was suffering from an attack of acute appendicitis. A greatly enlarged and inflamed cecum and inflamed appendix was found. No misgiving as felt that it was not case of acute appendicitis.

Three days after the operation, the patient began to have frequent loose motions to pass large quantities of bright blood with the motions and to suffer from severe general abdominal pains the incidence of which seemed to be greater on the left side of the abdomen.

After a month she was so emaciated, anemic, and ill that she was only kept alive by repeated transfusions of blood. Her hemoglobin value 13.10. The region of the large bowel was diffuse, tender.

A barium chloride diagnosed a small rectum and a rigid tube-like colon with no haustral markings (Fig. 3).

### SURGICAL MANAGEMENT

**Step 1.** Gas and oxygen anesthesia was used. A midline subumbilical incision was made. The colon from the cecum to the lower part of the sigmoid was found to be uniformly white opaque thick and rigid it presented all the appearances of an advanced stage of ulcerative colitis. The ileum was normal.

The ileum was severed at a point 4 inches from the ileocecal junction. The distal cut end was implanted in a stab wound in the right iliac fossa. The proximal cut end was implanted in the lower end of the subumbilical incision and the adjacent segment of ileum was given a wide application, by two rows of sutures, to the lowest part of the sigmoid and the rectosigmoid junction after the rectum had been drawn tensely out of the pelvis (the rectosigmoid reflexion of peritoneum is incised the rectum can be drawn well out of the pelvis) (Fig. 1). The sigmoid was cut across at a level that would enable its lower cut end to be implanted side by side with that of the ileum in the lower angle of the midline wound.

The upper cut end of the sigmoid was also implanted in the subumbilical incision.

The disposition of the patient's intestine now was she had a left sided enterostomy (rational surgical treatment for ulcerative colitis) the terminal ileum was so applied to the lowest part of the sigmoid and rectosigmoid junction that a rectoileal spur as constituted the crushing of which would make a rectoileal connection the proximal cut end of the ileum and the distal cut end of the sigmoid lay side by side in the lower end of the

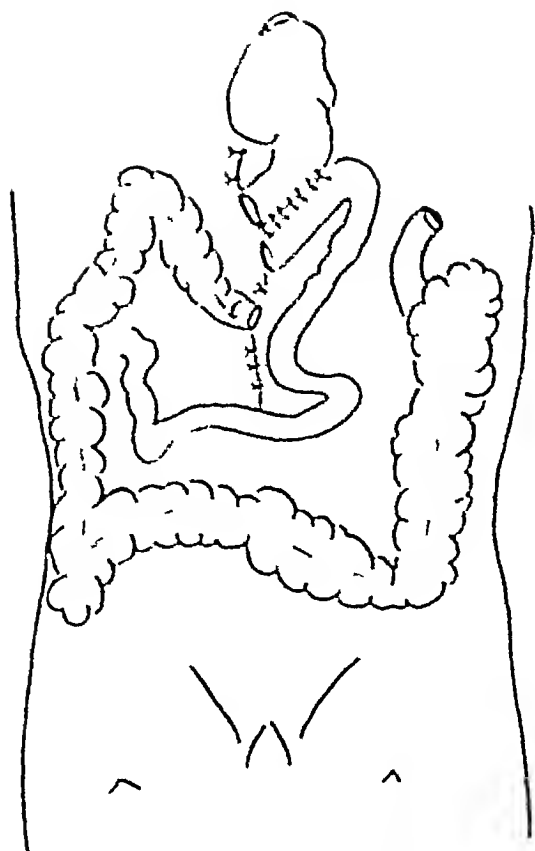


FIG. 1. Ileocecal junction.

central wound, and the colon except for a small segment at its left end was completely excluded, with an ileal opening in the right iliac fossa and a larger sigmoid opening in the left iliac fossa.

The excluded colon was crusted at two ends and healed out daily with an emulsion of cod liver oil containing sulfanilamide.

In 2 months the condition of the patient was generally good; no grossly improved, considerably pain and tenderness over the colonic region; pain and blood forming with enterocolic fermentation, no breath) passing from the small end of the excluded colon.

Step 2. In order to lessen the unpleasant effects of a fully functioning enterostomy on the abdominal wall and to begin the connection of the ileum to the rectum, the ileocecal sigmoid septum was crushed with an Oschner

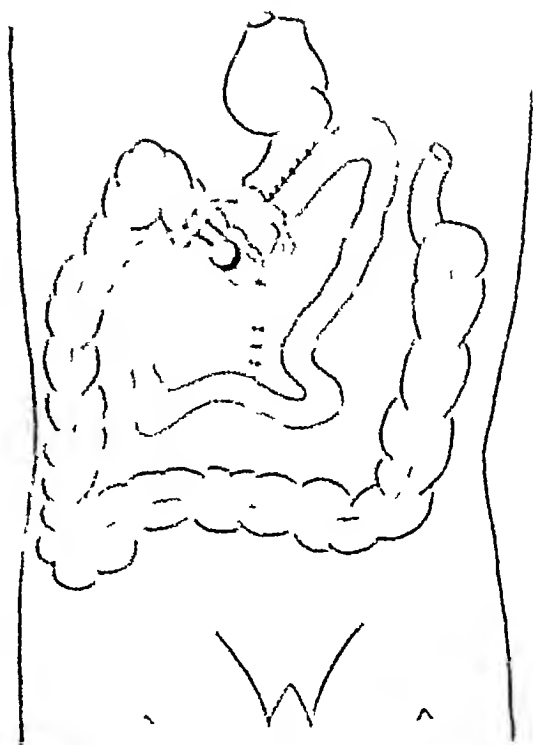


FIG. 2. Sigmoid septum crushed with Oschner's spatula.

DeBakey's spatula (Fig. 2). The by-pass was established into the rectum (in this case not very badly affected) permitted the passage of a quantity of intestinal contents into it, lessened the number of dressings, and soon arrested the excoriation of the abdominal wall.

Step 3. Two months later the patient's condition had so wonderfully improved that it was felt that the resistance of her tissues was good enough to close the bowel openings.

Accordingly, under local anesthesia, the cut end of the ileum and that of the lower end of the sigmoid were closed in layers and the abdominal muscles were loosely sutured over them. To lessen any strain on the sutures in the bowel ends a rubber tube was kept in the rectum for 2 weeks after the closure (the liquid contents of the small intestine passed very readily through this tube).

Further treatment of the excluded colon with sulfanilamide applications was prac-

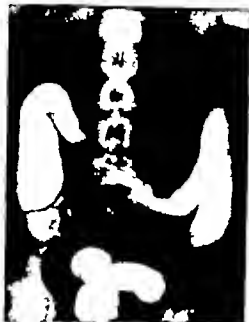


Fig. 3. Fluoroscopic ray showing small rectum and right half of colon.



Fig. 4. Resected colon showing the small bit of sigmoidum and the colon uniformly affected. The mucous membrane is uniformly thickened, of deep purple color and granular with pinpoint ulcerations uniformly distributed.

#### SUMMARY AND CONCLUSIONS

The surgical lessons arising out of this case are:

1. An unrecognized ulcerative colitis in its early stages may be the cause of severe and progressive ill health.

2. A patient with ulcerative colitis may come to operation in the guise of a case of acute appendicitis because the appendix, by virtue of its continuity with the cecum and colon, the subject of an acute or subacute inflammatory process.

3. A sliding scale, almost complete colectomy—in these cases the only operation of any value—can be carried out by a step by step surgical combined with medical treatment allowing ample time between each step to enlist the patient's natural recuperative powers, and designing the whole treatment so that a colectomy is the culminating aim.

In the case which has been presented a feet 9 inches of acutely inflamed diseased colon was removed and the relief and improvement was dramatic.

The patient is now, after 9 months, practically well. The rectum and the small amount of sigmoid left seem to give her a little pain.

This is an example of how an almost complete colectomy can be performed in circumstances which can scarcely be worse.

ticed and the patient improved rapidly. She still, however, complained bitterly of pain very definitely localized to the region of the excluded colon.

Step 4. Some months later when she appeared to be well enough to stand a colectomy, this final step in the surgical treatment was carried out under nitrous oxide gas and oxygen anesthesia. The operation caused the patient little disturbance. The length of colon removed was 2 feet 9 inches.

When the lumen of the colon was displayed the mucous membrane was seen to be uniformly involved from the ileocecal valve to the cut end of the sigmoid. It was of a ripe mulberry color greatly thickened and was pitted with pinpoint ulcerations. The muscle and peritoneal layer showed extensive chronic inflammatory infiltration. In this patient there still remains a small fraction of the sigmoid (about 2 inches). The rectum was not badly involved.

Figure 4 shows the appearance of the mucous membrane.

# POSTMETASTATIC SURVIVAL OF OSTEOGENIC SARCOMA

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THIS report discusses the patient from the standpoint of postmetastatic survival from osteogenic sarcoma in whom demonstrable *metastases to the lungs* alone are concerned. My own experience and that of others lead me to believe that once metastases from osteogenic sarcoma have appeared, usually in the lung where they are expected first, or in any other part of the body, the patient is in a hopeless condition. Parents and relatives are usually so informed. Sometimes amputation or local resection is refused after metastases are diagnosed because most patients die within a few months up to a year. In the Registry of Bone Sarcoma of the American College of Surgeons, there seems to be no clear cut instances of osteogenic sarcoma which have developed metastases in the lungs and in which patients have survived for a great length of time.

My patient has been kept under observation 13 years. The outstanding points I wish to bring out in the review are

1 A definite diagnosis of osteoblastic osteogenic sarcoma of the femur was made primarily by both roentgenological and histological examination

2 The leg was amputated well above the growth on the femur before any metastases in the lungs could be certified. The tumor was then clinically at least 9 months old and there had been one attack of cough with colored sputum, not examined

3 Amputation was performed after both femoral artery and vein were doubly tied through a separate incision, no constrictor was employed and the leg was very gently handled during operation

4 Within 10 months there was chest pain, bloody sputum, and roentgenological evidence and diagnosis of pulmonary metastases

5 There never developed any local or regional recurrence

6 The shadows of the pulmonary metastases for a few months seemed to multiply and increase in size, then reached a stationary stage which lasted for several years, finally changed slightly in density but not in size. The change in density might have been the result of improved roentgenological technique or better films

7 The roentgenological shadows of pulmonary metastases remain after 12 years

8 The patient is alive and as well as ever. He has maintained a more or less stationary weight for 10 years

9 There never has been any roentgenological, serum, or other type of therapy, except for one dose of suberythema x-ray which was given in 1930

10 The serum phosphatase has never been more than 14 units per 100 cubic centimeters since this method of examination has been used

11 His blood findings show only a secondary anemia

12 A careful restudy of the primary tumor confirms the diagnosis of osteoblastic osteogenic sarcoma. It is classed as a malignant tumor, it contains some areas with osteoid tissue, cartilage, and many mitotic figures

13 Although there have been intermittent attacks of cough with blood tinged sputum and many negative examinations for tubercle bacilli over the period of 12 years, no careful sputum examination attempting to find tumor cells in masses has been possible. No exploration of the lung has been performed to obtain tissue for biopsy, either by bronchoscopic examination, puncture, or direct thoracotomy

## CASE REPORT

J D, male, single, aged 21 years, born in Poland, where he lived the first 8 years of his life, was admitted to the Presbyterian Hospital, on May 7, 1929, with a complaint of painful swelling, which had existed for 9 months around and above the right

From the Presbyterian Hospital and the Surgical Department of the University of Illinois  
Read before the American Orthopedic Association, Johns Hopkins Hospital, Baltimore, June 3, 1942





Fig. Longitudinal section through the femur showing the tumor growth with its radiating characteristics and retained identity of the cortical margin in most part. The tumor mass fills the medullary cavity of the portion of the bone shown. Joint surface of the femur apparently is still unaffected.

knee. At that time he had lost 3 pounds in weight. The pain was continuous, increased by standing and by lying in bed, leading to insomnia but not completely disabling in walking. He had also in the last 3 weeks before admission experienced severe sharp pain in the right thigh and back with stabbing pain on deep inspiration. There was some cough considered to be the result of *lexxa* cigarette smoking accompanied by dusty and colored sputum.

The physical examination showed slender but male with normal findings except as follows: the abdomen was symmetrically rigid, condition said by him to have been constantly present. The liver seemed slightly enlarged to percussion but could not be palpated below the costal margin. No palpable lymph nodes were found. Wassermann reaction was negative.

The right knee region approximately twice the size of the left, presenting hard, irregular and some-

what tender swelling which seemed a part of the lower end of the femur. This leg could be flexed to right angle but could not be fully extended so that he walked with a limp from the contraction, standing fairly well with leg flexed to the knee. When the leg was forced passively beyond the range of normal motion pain was set up.

The urine was normal, the blood showed 65 per cent hemoglobin and 9,200 white blood cells. A roentgenogram May 8, 1930, of the lower half of the right femur and knee showed considerable soft part swelling with much new bone formation basally. The lower end of the femur extending outward in all directions from the shaft in a radial or ray-like arrangement. Shaft (old cortex) of femur slightly increased in density and the findings were considered to be those typical of osteoblastic osteogenic sarcoma. Two days later after the arteries of the amputated leg had been injected, a second roentgenogram showed a negative leg and foot and clear outline of the tumor of the femur. Found in the primary roentgenogram, its density increased apparently from the injection of the blood vessels by the opaque material used.

A best film May 9, 1930, as considered to be negative although a solitary dense nodular shadow was present in the left ilium suggesting enlarged gland or nodule in that position possibly small metastasis. Amputation was advised, with the belief that no surely demonstrated metastases had yet occurred.

On May 9, 1930 an incision was made over the popliteal triangle exposing the femoral vessels which were both doubly ligated and the small opening was sutured. A circular amputation of the upper third of the right thigh as then performed. The sciatic nerve as injected with absolute alcohol, and a rubber tube drain was left across the stump. A normal healing occurred and the patient left the hospital June 3, 1930.

The description of the amputated right leg on May 9, 1930 (Path. No. 20576, Case No. 3647) follows:

Gross. The specimen is the right leg of a young male removed through upper third of the thigh. The lower extremity is normal below the knee. A swelling is present from the knee joint up to and including the lower third of the femur. This tumor is firm, slightly discolored and firm. The thigh greatest circumference 146 centimeters and the same length of the swelling of the tumor is 15 centimeters.

An incision on the anterior surface of the thigh through skin, subcutaneous tissue, muscle and fascia reveals a grayish white nodular mass which anteriorly does not invade the muscles or fascia but has done so posteriorly. The muscle and overlying tissues move freely over the tumor mass. The knee joint is filled with dark fluid blood. The main nodular tumor mass has an irregular dull gray surface with various sized raised yellow masses extending from most numerous on the popliteal surface. The greatest circumference of the tumor is 20 centimeters.

the anterior length 13 centimeters, the whole covered by a translucent closely adhering capsule-like covering

A longitudinal section through the middle of the femur and tumor reveals on the cut surface a medullary cavity filled with hard, compact bone extending about 21 centimeters in length. There is a small cyst with irregular wall and border near the anterior extremity of this sclerosed cavity filled with dark, soft blood. The cut surface is not uniform in color but is principally white, irregularly spotted with faint brownish red areas, and is bonily rough. The outlines of the compacta of the femur are distinct and unobliterated. That portion of the tumor external to the outer cortical surface of the femur is softer than the portion within the medullary cavity and extends 3 centimeters beyond the edge of the cortex of the femur. This surface is dull and rough. The normal portion of the medullary cavity of the femur is filled with soft, dull, whitish red irregular marrow. The articular surfaces of the femur, tibia, and patella are normally smooth.

Microscopic sections through the tumor show a marked proliferation of mesenchymal tissue cells, the nuclei of which are oval and stain light purple. The cytoplasm is faintly pink and contains numerous processes which extend outward in the form of fibrils. Some nuclei show definite mitotic figures. There are scattered areas of pink-staining new bone.

On March 6, 1930, 10 months after amputation an examination showed a well healed thigh stump (he wore artificial limb), pain in the chest with coughing and expectorations of bloody frothy sputum. A chest roentgenogram this date showed numerous rounded, dense shadows and a second film on July 29, 1930, showed an increase in the number and size of these shadows. There was also present a uniform clouding of the left upper lobe of the lung which was interpreted to be a pressure atelectasis.

Subsequent roentgenograms at regular intervals have shown at first an additional number of metastases, with some enlargement of the older ones and then a resting stage in which the findings varied little, the calcified character of the nummular shadows within the lungs changing little in density, outline, or size. During the period from March, 1930, to April, 1942, the patient has experienced from time to time attacks of mild dyspnea, cough, bloody sputum, but no sustained loss of weight, he has led a fairly active life but has done no labor. Several times he has been picked up by the omnipresent social worker, who, told of his cough and bloody sputum, has insisted under our municipal laws covering suspect infection with tuberculosis, that he should report to the tuberculosis sanitarium for examination. Repeated examinations of sputa failed to reveal tubercle bacilli. There has been no radiotherapy and no change in diet over that normally taken by his family. His weight varied between 120 and 138 pounds, averaged 134 pounds.

An examination on January 10, 1942, gave a weight of 130 pounds. He still had some chest pains and had had some hemoptysis 3 months before, none



Fig 2 Roentgen film of specimen after amputation and injection of vessels. The ray like transverse projections of new bone formation seem typical of osteoblastic osteogenic sarcoma.

at time of examination. Stump scar and regional lymph nodes were normal. Roentgenograms, made of the skull, pelvis, and spine, were normal. The lungs still showed the same scattered calcific masses.

On April 10, 1942, 13 years after amputation and at least 12 years following the roentgenological demonstration of clinically diagnosed pulmonary metastases almost symmetrical in character in both lungs, no evidence of local recurrence in the stump or pelvic region has developed. The blood findings are red blood cells, 4,500,000, hemoglobin, 15.9 grams (99 per cent), and the white blood cells 14,100 with a differential count of neutrophils, 60 per cent, eosinophils, 2 per cent, lymphocytes, 34 per cent, and monocytes, 4 per cent. The serum phosphatase was 14 units per 100 cubic centimeters, a low adult average.

Pathologists believe that secondary tumors in the lungs are the result of direct nonmetastatic invasion or are true embolic metastases arising from malignant emboli carried into the pulmonary arteries. Both lungs are affected and pulmonary metastases found in about 30 per cent of fatal cases of malignant tumors.



Fig. Longitudinal section through the femur showing the tumor growth with its radiating characteristics and retained identity of the cortical margin in most part. The tumor mass fills the medullary cavity of the portion of the bone above. Joint surface of the femur apparently is still unaffected.

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Gross. The specimen is the right leg of a young male removed through upper third of the thigh. The lower extremity is normal below the knee. A swelling is present from the knee joint up to and including the lower third of the femur. This tumor is fusiform, slightly discolored, and firm. The thigh girth circumference 36 centimeters and the lower length of the swelling of the femur is 15 centimeters.

An incision on the anterior surface of the thigh through skin, subcutaneous tissue, muscle and fascia reveals grayish but nodular mass which tenaciously does not invade the muscles or fascia but has done so posteriorly. The muscle and overlying tissues move freely over the tumor mass. The knee joint is filled with dark fluid blood. The mass of the tumor mass has irregular dull gray surface.

The mass is raised, yellow mass is studied by the most aneurysm on the popliteal surface. The greatest circumference of the tumor is 29 centimeters.

the anterior length 13 centimeters, the whole covered by a translucent closely adhering capsular like covering.

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An examination on January 19, 1942, gave a weight of 130 pounds. He still had some chest pains and had had some hemoptysis 3 months before, none



Fig. 5. Roentgen film of specimen after amputation and injection of vessels. The ray like transverse projections of new bone formation seem typical of osteoblastic osteogenic sarcoma.

at time of examination. Stump scar and regional lymph nodes were normal. Roentgenograms made of the skull, pelvis, and spine were normal. The lungs still showed the same scattered calcific masses.

On April 10, 1942, 13 years after amputation and at least 12 years following the roentgenological demonstration of clinically diagnosed pulmonary metastases almost symmetrical in character in both lungs no evidence of local recurrence in the stump or pelvic region has developed. The blood findings are red blood cells, 4,500,000, hemoglobin, 15.0 grams (99 per cent), and the white blood cells 14,100 with a differential count of neutrophils, 60 per cent, eosinophils, 2 per cent, lymphocytes, 31 per cent, and monocytes, 4 per cent. The serum phosphatase was 1.4 units per 100 cubic centimeters, a low adult average.

Pathologists believe that secondary tumors in the lungs are the result of direct nonmetastatic invasion or are true embolic metastases arising from malignant emboli carried into the pulmonary arteries. Both lungs are affected and pulmonary metastases found in about 30 per cent of fatal cases of malignant tumors.



Fig. 3. Roentgen film of chest May 2, 1939, before aspiration. Only one suspicious area in the left upper lobe, as considered as "possible metastasis," but after additional study it was believed not to be such.



Fig. 4. Roentgen film of chest March 8, 1940, after aspiration shows multiple areas of calcification in both lungs, which are diagnosed as osteogenic or osseous metastases.

In osteogenic sarcoma blood borne pulmonary metastases occur in approximately 60 per cent of the fatal cases. As in other homogeneous tissues, most metastases are spherical in shape and quite sharply circumscribed, but when they occur in the subpleural area they may spread out in plaque like or stellate growths which may encase the lung as so well recorded by Le Count in 1909.

Ossifying pulmonary metastases of osteogenic sarcoma may contain areas of dense osteoid tissue or fully formed bone which may undergo degenerative changes when the secondary growth is large. These changes include yellow caseation, hemorrhages, liquefactive softening and prostatic infections. Calcification in a secondary growth may follow by discharge of a portion of it through a bronchus but this seldom is seen as compared to this finding in primary tumors of the lung.

A progressive multiplication of malignant tumor cells is the main factor in neoplastic infiltration—successive generations of cells are continuously budded out into surrounding tissues, and Willis warns that one must not

rely too much on the motility of tumor cells and also recalls that their phagocytic powers are debatable. Certain biological factors may appear in the growth of secondary pulmonary deposits.

a. Soluble metabolites, capable of affecting surrounding tissues may expedite or pave the way for tumor invasion. In carcinoma a high lactic acid output has been found but there is no direct evidence that these products have any lytic or other damaging effects on the surrounding tissue.

b. Mechanical pressure from the secondary growth might set up degenerative or other damaging effects in the cells of the tumor invaded tissues.

c. Tumor cells may form specific heterolytic ferments but that the respiratory tract contains no digestive enzymes is a known fact.

d. Changes in tissue tension, dioxide and carbon dioxide content, or circulation may affect metastatic growths.

e. Changes in hormone or enzyme content of the serum are said to affect secondary malignant tumor deposits as in bone.



Fig 5 The chest September 22 1937 There seems to be some change in the shadow just to the left of the heart as if a cavity or absorption of calcified material had occurred Other masses in lung appear about as 7 years previously



Fig 6 The chest January 19, 1942 There may be slight change in the various nodules seen in the lungs expressed in the film by density variation On the whole the picture is nearly identical with previous findings

However, malignant tumors retain a remarkable stability of type. Structure of the last formed secondary growths is in most instances very similar to the original tumor, even in minor details. Ewing says that in general there is a gradual loss of structure in metastatic tumors.

Some of the emboli of tumor tissue or cell masses in the lung may not grow but remain sterile and are absorbed or disappear, hence tumor embolism is not always true tumor metastasis. By penetrating pulmonary veins, they may become the source of systemic metastases leading to deposits in other tissues, as of the liver, brain, spleen, and of other organs as well as of other bones such as the spine and skull, and yet very little, if any, evidence of the first pulmonary metastatic growth may ever be either suspected or diagnosed clinically.

In discussion of delayed growth of metastatic tumors, Willis states that the majority of malignant tumors pursue a steady and uninterrupted course to a fatal termination, but that exceptions do occur as

1 Tumors which, though frankly malignant in type and production of metastases, exhibit long duration with little or no impairment of the patient's health,

2 Tumors which, following surgical removal, recur locally only after a long period of freedom from disease,

3 Tumors which, in spite of completely successful local treatment followed by a long period of health, recur as metastases,

4 Tumors which exhibit spontaneous retrogression, partial or complete, *in their primary or metastatic situations*

I believe that the patient here reported may fall into this first group. I have had others, with osteogenic sarcoma, who were in the third group, coming to death from metastases recognized after years, in other bones or organs, not always in the lungs—possibly on account of the reasons stated.

Chemical methods of early determination of metastases and a hope of restraining them were implied in Coley's reports in 1908 of 430 instances of varied types of sarcoma treated by mixed toxins, 28 of which had passed

through a period of 3 to 15 years since the disappearance of the tumor. He believed that the chances of success are certainly much higher after use of the toxins than the general percentage of 11 per cent of recoveries derived from his total series.

The transfer of a given type of cell from its origin in mesoblastic or other tissue by metastasis to lung or intestine might modify its exposure to circulation, dioxide and carbon dioxide supply. This change might lead to a more rapid maturation of the cell type involved, and in metastases from osteogenic sarcoma lead to a more rapid calcification, i.e., a more rapidly maturing form of the cells which might lessen or modify its malignant power in the new locus. In presence of calcification the malignant character of the active cell of the tumor, the true new-growth cell might be throttled down or strangled. Consequently these metastases after reaching a certain size might cease to grow further. They may remain stationary and act simply as foreign body deposits relatively innocuous, with decreased blood supply, often surrounded by a fibrous envelope in pulmonary tissue. Another factor includes a change in the host's resistance as influenced by his reaction to the numerous metastases—a favorable or enhanced reaction aiding in limiting the amount of toxicity from the new-growth without systemic expressions such as loss of weight, nutrition and strength but with the development of antibodies which would aid in suppression of the spread of secondary deposits.

Maturity of the gonads might furnish an increased amount of hormone (testosterone) which likewise would act as a suppressor. Much experimental work on the effect of hormones on metastasis in man or transplanted tumors in mice has already been performed. Completely accepted and stabilized results which can be relied upon for clinical use have not yet been forthcoming. Huggins in his last paper is enthusiastic about reduction or obliteration of metastases from carcinoma of the prostate treated by orchidectomy. We have known for some time that metastases may be delayed or rendered less painful or even caused to diminish when treated by intensive roentgen therapy. One factor here may be that the

roentgen ray may destroy the secreting power of the testis during this treatment and orchidectomy, as far as active hormones are concerned may thus take place. Some urological surgeons, for example Kretschmer, do not favor this radical operation but use methyltestosterone in quite large doses in an effort to suppress action of testosterone and thereby negate its effect, believing that they obtain clinical subsidence and improvement, certainly diminution of pain in the bone metastases.

Since Key's report on osteogenesis imperfecta (1926) the enzyme phosphatase has been found in the kidney, intestine, blood, bone, and other tissues. It possesses a remarkable action best in a hydrogen-ion concentration of about 8 and with the presence of inorganic phosphate. Bodansky and Jaffe found that serum phosphatase is elevated in disease associated with excessive bone formation, and it has been stated (Woodard) that the elevation of phosphatase is proportional to both the degree of osteoplasia and the rate of growth of the tumor. This seemed to be a hopeful avenue of approach to diagnosis or even prognosis of bone metastases from osteogenic sarcoma. It was believed that while an elevation of phosphatase is not a specific test for bone cancer, a very high serum phosphatase in osteogenic sarcoma usually indicates an extremely malignant tumor, whereas a low serum phosphatase indicates a slow growing and relatively benign tumor. Huggins is inclined to agree with this. However, serum phosphatase of nonosseous origin is raised by diet high in carbohydrates also in obstructive jaundice, whereas it is lowered by starvation or high protein diet.

A rise in serum phosphatase in some types of bone tumors is apparently caused by an overproduction of the enzyme by neoplastic tissue or adjacent periosteum and a removal of part of the enzyme by the blood stream. Malignant disease *per se* does not influence serum phosphatase. In 20 patients with benign bone tumor and osteomyelitis only 1 showed an elevated serum phosphatase (an aggressive giant cell tumor laying down bone). This suggests that bone forming characteristics of a tumor are of more importance than its malignancy in determining whether its

presence will give rise to an elevated serum phosphatase. The best example is Paget's disease, which always has a high phosphatase. In 14 instances of malignant disease not primary in, but metastatic to, bone, a high phosphatase was found ranging from normal to 45.5 the highest in metastases from carcinoma of the prostate and in the osteoblastic type of tumor. In osteolytic types of osteogenic sarcoma, in chondrosarcoma, and in endothelial myeloma, serum phosphatase may be normal or only slightly raised. However, in the case here reported in which the metastases were numerous and osteoblastic in type one might expect a high serum phosphatase, which was not found. Consequently, a correlation between serum phosphatase figures and the histological and radiological type of tumor does not seem close, and the phosphatase findings can be considered only as suggestive rather than definitely diagnostic of the type of tumor being studied. In theory also there might be an interpretation of the prognostic significance of phosphatase determination inasmuch as when an osteogenic sarcoma is present forming large quantities of serum phosphatase absorbed into the blood stream, removal of the tumor by operation (amputation or resection) or its inactivation by radiation or toxins should result in a fall of serum phosphatase. One might feel that the extent and constancy of the expected drop would be an indication of the effectiveness of the treatment—a late rise in serum phosphatase indicating the presence of recurrence or metastases. Clinical study of patients does not seem to back this up and little reliance can be placed on phosphatase determination as an aid in prognosis or of value in detecting pulmonary metastases. Healing callus about a pathological fracture resulting from osteogenic sarcoma might cause a high serum phosphatase.

Woodard and Hignbotham have studied the use of serum phosphatase determination as a help in evaluating radiation therapy of bone tumors for amputation either as an elective measure or while awaiting consent for surgical removal of the tumor. A tumor going on and spreading would be expected to give a continued raised phosphatase. Clinical tests of this method fail to show reliable results, al-

though with added cases some help may be derived from this source of estimation and a failure of serum phosphatase to fall after amputation with or without radiation may be found due to residual portions of the tumor or undiscovered metastatic deposits.

These authors previously expressed an opinion that when a high serum phosphatase level is found associated with tumor showing little new bone formation, the rate of growth has outstripped the rate of deposition of calcium phosphate—which might be a restatement of our rather long standing clinical dictum that the rapidly growing lytic action tumor is the most malignant. Tissue phosphatase determination after amputation may help decide the point. They have employed radioactive phosphorus in treatment believing that the tumor picked it up and thus obtained local radium treatment. If the embolic masses from an osteogenic sarcoma will take up the radioactive phosphorus as readily as the parent mass, they propose its use to weaken these small groups of cells enough to prevent them from becoming established and from forming lethal metastases.

The patient reported here shows little spontaneous regression of tumor and metastases. Spontaneous cures do follow carcinoma and even laboratory animals developing transplanted tumors may recover. Age, rapidity of development, and virulence of the tumor, interference with blood supply, febrile processes, artificial menopause or incomplete operations, are factors in these regressions, and the growth energy of the particular tumor must be considered. Handley said "The process of cancer is normally accompanied by regressive or curative processes. The recorded cases of natural repair of cancer, far from being anomalous and exceptional, merely illustrate more strikingly than usual the natural laws which govern every case of the disease."

In current parlance our patient seems to have something which is holding back the fatal termination of a disease we have come to dread as possessing a high mortality. Why could we not transfuse his blood into a patient with known osteogenic sarcoma and just beginning metastases to observe whether deterrent or curing effects followed? Such a patient has



just been in the hospital with known small metastases in the spine and lungs, but my patient departed for the summer before arrangements could be made for this test. Finally if any group of such patients with prolonged life after known metastases from osteogenic sarcoma could be found their blood might be given to a common blood or plasma bank to be used as a therapeutic agent in other patients with incipient stages of the disease.

## REFERENCES

- BODANSKY A and JAFFE, H. L. Arch Int Med, 934, 34-35.
- COLLEY W. B. Boston M. & S. J 906, 38 73
1. COMELAND M. M. Surgery 912, 495.
4. DORRICK, J. L., and DE ROUVILLE, W. H. Arch Surg, 94, 43 995.
5. FRANKFURT, C. C., and McLELLAN, R. Am. J. Cancer 935, 24 899.
6. G. FLEISS, H. R. and CROWDER, G. H. G. Surg. Gyn. Obst., 1906, 615.
7. HEDGECOCK, CHARLES. The treatment of sarcoma of the prostate. Paper delivered before American Surgical Association, April 7 1942.
8. KA. H. D. J. Biol. Chem., 1930, 87 235, 240.
9. KEY J. A. Arch. Surg. 924, 5 511.
10. KOLODNY, ARTHUR. Surg. Gyn. Obst., 17- Suppl. 1.
11. LE COQ, E. R. Johns Hopkins Hosp. Bull., 12 30 36.
12. RHODANDECK, G. L. J. Cancer Res. 1942, 3 49.
13. SCHMIDT, C. C. Surg. Gyn. Obst. 1938 64 1.
14. SCHMIDT, C. C., and F. SCHMIDT, C. C. Ann. Surg. 935, 102 555.
15. WACHSBERG, L., and POOL, H. Manch. and West. 9 5 73 3.
16. WELLS, H. G. Arch. Int. Med. 9 6, 3 34.
17. WELLS, R. A. The Spread of Tumors in the Body. London J. & A. Churchill, 1934.
18. WOODWARD, HELEN Q. and HARRINGTON, X. L. J. Am. M. Assn. 94, 16 52.
19. WOODWARD, H. Q., GR. H. T. CHERRY, and CART. B. L. J. Clin. Invest. 996, 5 91.

# THE GASTRIC MUCOSA AS AN ENDOCRINE GLAND

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THE therapeutic status of the patient with serious gastric ailments has been very little improved during the past two decades. Progress has been retarded due to the lack of knowledge concerning the relationship between gastrointestinal physiology and pathology, and the consequent inability to correlate the progress of disease processes in this important organ. The development of new methods of investigation into gastric physiology in humans and animals and the segregation and synthesis of several hormones have lent impetus to an additional conception of gastric mucosal activity. We believe it will prove helpful in explaining important pathological changes and lead to scientific curiosity and therapeutic advancement. The arbitrary division of digestion into chemical and nervous phases, although correct, in so far as it goes, is not sufficiently comprehensive of the physiological scope of the gastric mucosa, and therefore insufficient in explaining the pathological states which ensue. Up to the present time our attempted therapy in gastric ailments, both benign and malignant, has been notable for too frequent failure.

In recently published reviews on gastric carcinoma we called attention to the age incidence and sex discrepancy in this condition and suggested an endocrine basis. The new field of inquiry opened to gastroenterologists by the recently isolated and synthesized sex hormones was pointed out by Abrahamson and Hinton (1) and Hinton (30).

In an effort to correlate the marked changes in the content and character of the sex hormones which takes place during that period when gastric carcinoma is most prevalent, with the effects of age and sex on the physiology and pathology of the gastric mucosa, we reviewed those cases of benign gastroduodenal lesions which we had available. In the past 15 years, 1171 cases of peptic ulcer have

been registered, studied, and followed in the gastroenterological clinic of the medical and surgical services of the Fourth Divisions of Bellevue Hospital. Of these, approximately 10 per cent (112 cases) have been surgically treated and the remainder of the patients not operated upon carried under medical care. In reviewing age incidence and sex distribution of these cases, it was found that approximately 88 per cent (1,043) were males and only 12 per cent (128) were females, approximately 9 to 1. The incidence of duodenal ulcer was 89 per cent and of gastric ulcer 11 per cent (approximately 9 to 1). During this 13 year period approximately 337,500 males and 247,500 females were admitted to the Bellevue Hospital Medical and Surgical Clinics, a ratio of less than 3 males to 2 females.

Several recent reviews of large numbers of peptic ulcer cases showed a similar sex discrepancy. Collected data of approximately twenty-one authors, including all types of peptic ulceration, show an incidence of 8 to 9 males to one female, Nicholson and Miller and Miller and Elsom. McMullen, on reporting the x-ray findings in 4,400 peptic ulcers, noted the great preponderance of males and found that females reached the peak of incidence in the fourth and fifth decades and the males in the fifth and sixth decades. Our age incidence differs from this observation.

In view of the sex-linked character of this disease, we decided to re-examine the known effects of hormones on the gastric and duodenal mucosa and to add to this the clinical and experimental data we have gathered to date. Although we have had some experience with various hormones in the treatment of gastroenterological conditions, we have decided to present only those in which the follow-up has been of sufficient time (1 to 5 years) to make the observations of value.

For several years medical literature has contained clinical and experimental reports on the effects of the isolated hormones and vita-

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mins on the stomach and duodenum. In our attempt to collect and summarize this knowledge of hormonal effects on the gastroduodenal mucosa, we realize there are many omissions due to the limitations of time and space (inherent in an article restricted in size and scope).

The means by which the mucosa of the pyloric end of the stomach affects the production of secretions from the cardia and fundus have not as yet been completely established but there is sound experimental evidence to show that the hormone gastrin Edkins (20-21) and Koch Luckhardt and Keeton (38) is produced and thrown into the blood stream by the pyloric mucosa. Because of the similar action of histamine upon the gastric mucosa, several authors believed this hormone to be histamine however recent work on isolated and denervated gastric pouches with histamine-free extracts demonstrates the true hormonal character of the internal secretion of the gastric mucosa (Friedman, Gray (38) Babkin, and Best and Taylor).

Although some of the fundamental physiological aspects concerned with the "gastrin" hypothesis remain unsolved experimental evidence accumulated during the last few years seems to indicate rather definitely that the mucosa of the pyloric portion (of the stomach) is responsible for the endocrine secretion of the gastric mucosa. Hormones from the Intestine secretin (Ivy 33) cholecystokinin (Ivy 34) and enterogastrone (Friedman) also affect the gastric mucosa. It has been shown that the internal secretion of enterogastrone, which depresses gastric secretion (Day and Komarov) activates and stimulates the duodenal mucosa.

Recent experiments and clinical findings show that the gonadotropic substances in the blood stream influence the activity of the gastric mucosa. The anterior pituitary like fraction of pregnancy urine depresses gastric secretion (Culmer Atkinson and Ivy and De Lisl) believed that the depression of gastric secretions following the administration of anterior pituitary like substance is secondary to its effect upon the thyroid and ovaries.

Increased acid secretion in dogs has been noted in transplanted gastric pouches during

lactation (Klein). Gastric hypersecretion has been noted following parturition (Hollander). Gastric acidity is reduced during pregnancy. Peptic ulceration rarely occurs during this period and if it was present prior to gestation, a remission usually takes place (Arm. r. Strauss and Castle). This was thought to be due to increased blood estrogen (Winkelstein, 7) but further observations following estrus-infections in animals and humans have failed to verify this finding (Atkinson and Ivy).

It is a fundamental tenet of the concept of internal secretion that the endocrine organs secrete chemical hormones which have specific effect, whether their action is on other endocrine organs, or a tissue group, or on all the tissues of the body. Since we assume that the gastric mucosa has an internal endocrine secretion into the blood stream as well as an external endocrine secretion, it should be considered as an hormonal gland and its activity subject to the changes which effect other similar glands. This conception will allow for the study and explanation of physiological and pathological changes now obscure.

#### INTERRELATIONSHIP OF HORMONES AFFECTING GASTRIC MUCOSA

There is ample evidence to show that thyroid activity has a definite effect on the sex hormones. Thyroxin suppresses estrus, and estrogen depresses the thyroid while androgen does not have this effect. Thyroxin increases the activity of the gonadotropic factor Melnik (44) points out that there is a thyroid gonad effect in addition to the pituitary-gonad effect.

It is important to note that the corpus luteum hormone, progesterone is the only hormone present in females which has not been found in males. It promotes the renal excretion of estrogen (Smith and Smith 67), and has a corticominimetic action (Wells and Greene). There can be no doubt that it has a definite effect on the general hormone balance and is a factor in the estrogen-androgen ratio stabilization in the female. Attempts have been made to establish its relationship to gastric mucosal activity (Manville and Munroe) but no proof of this action is as yet forthcoming.

Hormones in the blood stream not only have a definite effect upon other hormonal gland activities, but also are related to the nature and content of several of the mineral and chemical constituents in the blood plasma. In normal girls at puberty, the calcium and nitrogen balance is depressed by the administration of estrone (Johnston). In premenopausal and postmenopausal diabetic women, estrogen lowered the insulin requirements (Spiegelman). The excretion of sodium chloride and retention of potassium is influenced by injections of testosterone proportionate (Kenyon, Sandiford et al, 36).

#### RELATIONSHIP OF ENDOCRINE TO VITAMIN ACTIVITY ON GASTRODUODENAL MUCOSA

The information on vitamin is quoted to show the close linkage between vitamin intake and hormone activity. It is known that the anabolism and metabolic activity of many endocrines are dependent upon the presence of various vitamins, either as an integral part in its metabolism, or as an intermediary link in the resulting activity.

Most have agreed that vitamin C plays a fundamental rôle in the process of wound healing. The close relationship between the adrenal glands and vitamin C storage and their general effect upon epithelial growth and body metabolism have been pointed out by Murlin (54). Although the adrenal cortical hormone was found to have no demonstrable replacement activity in experimental avitaminosis B, the apparent partial replaceability of vitamin C by adrenal cortical preparations reported by several observers is due to the presence of ascorbic acid in such extracts. Crystalline vitamin C is more effective when administered intraperitoneally than by mouth. The other considerations which have led various observers to assume the existence of an intimate relation between the adrenal cortex and vitamin deficiencies are explicable on the assumption that the hormone and vitamins are necessary for the proper functioning of a great number of organs and tissues (Grollman and Firor). Hunt believes that vitamin C deficiency is common in patients suffering from peptic ulcer and from carcinoma of the stomach.

The presence of large amounts of vitamin E in neoplasms of the gonads and a close relationship between vitamin E and estrogens have been claimed. Although several workers dispute the directness of this relationship, these refutations have been recently answered by Shute.

Although to date insufficient corroborative work to prove this contention is available, vitamin H (biotin) causes a lowering of metabolic rate and a recession in tumor growth. Induced biotin deficiency gives a possible explanation to the occasional spontaneous recession in malignancy. The experimental work on rat primary liver carcinoma induced by feeding "butter yellow" and its relationship to biotin is interesting but not conclusive (West and Woglon).

Two hundred patients with peptic ulceration were given large doses of vitamins A and D in the form of cod liver oil concentrate of high vitamin content (approximately 50,000 units of A and 12,000 units of D per ounce). This was administered 1 ounce three times a day. Although these patients showed subjective and objective improvement, gain in weight, reduction in pyrosis, abdominal pain, etc., they all required further medication for the control of their gastrointestinal symptomatology and no specific effects on the gastric mucosa could be noted.

Forty patients all with positive x-rays for peptic ulcer were placed on 6 gram tablets of yeast concentration containing at least 50 international units of B<sub>1</sub> and 50 Sherman units of G, 2 tablets three times a day were administered. Other factors in the vitamin B complex were present, but their exact unitage was not noted. Although there was an increase in weight, appetite, and improvement in their general health, the great majority required further medication, and no specific information concerning its effect is forthcoming.

Eighteen patients were placed on cevitic acid (vitamin C) 25 milligrams, three times daily for 2 to 4 week periods. No extraordinary clinical or roentgenographical improvement occurred in this group with the exception of 2 patients whose symptoms seemed completely alleviated clinically and by x-ray. On closer examination, both of these patients proved to

TABLE I.—RESULTS IN TWENTY FIVE CASES OF PLETTIC ULCERATION TREATED WITH THYROID AND THYRONIN

No.	Age	Duration of symptoms (years)	X-ray picture (normal)	R. A. C.	Thyroid (grs. daily)	Thyroid (grs. weekly)	Thyroid (grs. daily)	Thyroid (grs. weekly)	3 mo.—4 mo. follow up	6 mo.—1 year follow up	1 year—2 years follow up	Remarks
1	34	3 1/2	Dis +	++	+	+	+	+	Unimproved	Improved	Unimproved	Worsening spinal fluid +
2	40	3 1/2	Dis +	+	+	+	+	+	Unimproved	Improved	Unimproved	Exacerbated spinal fluid +
3	40	10 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
4	41	3 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
5	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
6	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
7	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
8	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
9	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
10	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
11	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
12	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
13	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
14	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
15	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
16	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
17	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
18	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
19	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
20	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
21	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
22	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
23	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
24	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +
25	41	1 1/2	Dis +	+	+	+	+	+	Unimproved	Unimproved	Unimproved	Exacerbated spinal fluid +

Thyroid tablets were given in 100 mg. capsules, 2 capsules 3 times a day. Thyronin tablets were given in 100 mg. capsules, 2 capsules 3 times a day. The results were recorded as follows: +, improved; -, unimproved; ++, greatly improved; ---, no change.

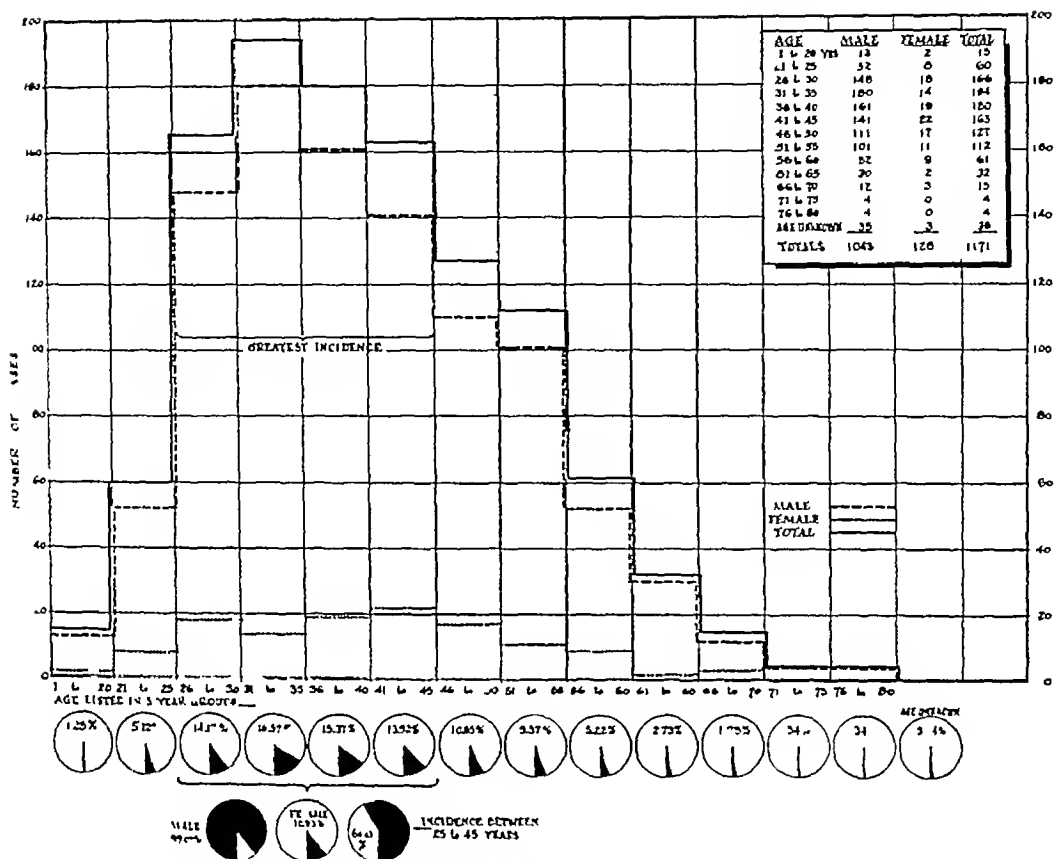


Chart 1 Showing sex and age incidence in peptic ulcer patients

have subclinical scurvy as a result of prolonged stringent ulcer diet during and prior to coming for treatment. Since additional medication was required in 16 patients no definite information on the gastroduodenal mucosa can be derived from this group. Several of the patients were given parenteral injections of crystalline ascorbic acid in addition to the oral administration, with no further beneficial result.

Our previous work on epigastric symptoms in hypothyroidism (Hinton) showed that the gastric hypermotility which accompanied abdominal pain in this condition could be relieved by the administration of thyroid. Moelbig believes these patients are benefited by thyroid therapy because of the thyroid-hypothalamic-gastrointestinal relationship. While an enormous but inconclusive literature

exists on the relationship between the gastrointestinal tract, thyroid gland and sex glands, recent studies by Marine and Rosen have shown a direct relationship between Graves' disease, myxedema, and androgen-estrogen excretion. We have followed a group of 25 patients, all suffering from peptic ulcerations (x-ray positive), who have been placed on combinations of thyroid,  $\frac{1}{2}$  to 1 grain three times a day, by mouth, and thyroxin intravenously  $\frac{1}{60}$  grain weekly. In an attempt to confirm specificity of the actions of these drugs on the gastrointestinal mucosa and eliminate rise in basal metabolic rate, some of these patients were placed on dinitrophenol. We fully realize the difficulties in the scientific interpretation of results of this type of clinical experimentation, the dangers of drawing false conclusions are obvious.

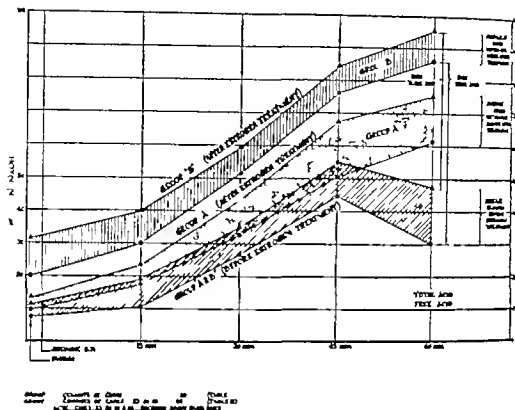


Chart 1. Graph showing increase in gastric acidity after estrogen treatment.

The basal metabolic rate in this group was within normal limits. There were 4 female and 11 male patients. Three patients had been operated on and showed marginal recurrent ulcerations having had gastroenterostomies, and 1 a gastric resection 2 to 3 years previously. Results of gastric analysis done prior to and following treatment showed that any changes which occurred were within the percentage of error (At the end of the 3 months follow-up 6 patients were cured, 4 both symptomatically and by x-ray report 5 patients were symptomatically improved but the x rays remained positive. A total of 10 patients seemed improved by medication at a 3 months follow up. During the following year there were 7 patients who had recurrences of their acute symptoms and one with perforation. Several of the patients improved on later examination became unimproved and 2 came to operation.)

In an effort to determine whether any of the improvement noted was due to a simple increase in basal metabolic rate, 5 of the improved cases and 4 of the unimproved cases were placed on dinitrophenol,  $\frac{1}{2}$  to 1 gram three times a day for a period of 1 to 3 months. No difference was noted in those placed on thyroid and those placed on dinitrophenol. Although it is hardly possible to state from these clinical and x ray results the total effect of thyroid and thyroxin upon the gastric mucosa, we can observe that the results both therapeutically and upon the course of the pathological condition were poor and variable and about equal to a controlled group on other forms of therapy for peptic ulcer.

Several effects of sex hormones on the gastrointestinal mucosa have been noted. Interest has been stimulated to attempt to correlate the relationship between the ductless glands and peptic ulcer. Sandweiss and a-

ciates have collected data to substantiate the observation that pregnant women are seldom afflicted with peptic ulcer and concluded that the anterior pituitary-like hormone depressed the gastric secretion and was a protective factor against peptic ulcer Winkelstein (74) treated a group of 20 menopausal patients having ulcer symptoms with estrogen. His results were inconclusive and it was not possible for him to determine whether this was a specific effect on the gastric function or whether it was a secondary effect brought about by a general symptomatic improvement due to relief of the neurovascular symptoms of the menopause. Others believe that the posterior pituitary gland is implicated in the production of peptic ulcer. Experimentally they report that the removal of the posterior portion of the pituitary gland of dogs increased gastric secretion after histamine injection and inhibited gastric secretion with large doses of pituitary (Metz and Lackey).

In an attempt to ascertain the effect of estrogens on the activity of gastric and upper intestinal mucosa, we have placed 29 males with peptic ulcerations of the duodenum on various dosages of estrogenic substance (theelin in oil).

In each case from 13 to 31 injections were given, 6,000 to 50,000 international units being given daily intramuscularly. A careful investigation of the clinical history and physical findings together with laboratory data such as repeated x-ray examinations, gastric meal tests, hematological studies and gastroscopy, and blood and urine studies for estrogen determinations were performed. These cases have been carefully followed over a 1 to 5 year period.

All 29 patients were males, average age 39.2 years. All patients had positive x-rays for duodenal ulcer. The average length of time since the diagnosis was established and the patient was placed under treatment in this clinic was 2.9 years (several patients had refused operation).

Injections were given 6 days per week, intramuscularly (buttocks).

Of the 29 cases, 28 were followed for 1 to 3 months, 21 for 6 months to 1 year, 18 for 1 to 3 years, and 11 for 3 to 5 years.

Clinical results	X ray
28 cases followed for 1 to 3 months <sup>1</sup>	
1 recurrence of severe symptoms (worse)	less 9 negative x rays following treatment
1 unimproved	plus 17 positive x rays following treatment
8 good results Mild residual gastrointestinal symptoms	plus 3 evidence of healed lesion, with no activity
15 asymptomatic following treatment	
1 results unknown	
21 cases followed 6 months to 1 year	
6 recurrences of severe symptoms	less 1 negative
4 unimproved	plus 18 positive
6 good Mild residual gastrointestinal symptoms	10 unknown
4 asymptomatic	plus evidence of healed lesion, no activity
9 results unknown	
19 cases followed 1 to 3 years <sup>1</sup>	
7 further recurrence of symptoms	less 3 negative
11 cases in all had recurrence of symptoms	plus 14 positive
2 unimproved	plus 1 evidence of healed lesion, no activity
5 good results Mild residual gastrointestinal symptoms	
2 asymptomatic	
2 operated upon (1 asymptomatic) (1 dead after operation)	
11 cases followed for 3 to 5 years	
2 further recurrences of symptoms	less 3 negative x rays (2 operated cases)
8 cases in all had recurrence of symptoms	plus 8 positive
3 good	
3 asymptomatic	
3 unimproved	
1 operated upon (asymptomatic)	

<sup>1</sup>Two cases with former good results and recurrence had no further injections each 1,000 units of theelin 10 and 12 months respectively after the original injections. These patients are reported as good or improved but with occasional gastrointestinal upset and unimproved respectively 1 to 3 years following treatment.

Twelve patients were given gastric test meals both before and after treatment, in 7 (group A) the second test was performed at varying intervals following treatment (2 weeks to 1 month). Although several were above normal limits prior to treatment, the free and total acid either remained above normal or was perceptibly higher following treatment. No cases showed a fall in either free or total acid despite clinical and x-ray improvement.

In 5 cases (group B) gastric test meals were performed 1 day to 1 week prior to theelin injection. The method of gastric analysis employed was as follows:



The patient came in without breakfast. A Levine tube No. 18 was passed through the nose into the stomach, and a fasting specimen of about 30 c.c. collected and labeled as such. A test meal specimen of about 30 c.c. was then taken and labeled No. 1 and after that at 15 minute intervals additional specimens, to a total of 4 were collected and labeled No. 2, No. 3 and No. 4 respectively.

In group B 3 cases showed a moderate degree of hyperacidity and 2 cases showed normal gastric acidity prior to estrogen injections. All showed a tremendous increase in free and total acidity following the injections of estrogen. Increase of 40 to 180 per cent free acid and an increase of 23 to 164 per cent total acid (Chart 2).

We are fully aware of the many difficulties and pit falls present in attempting to evaluate the results of any treatment for peptic ulcer. Spontaneous remission is a characteristic of this condition. However our cases were selected because of their chronicity and their lack of response to other forms of therapy. We have under treatment several groups of patients who act as controls and who have been receiving oral and parenteral medication during the same period. Of 29 cases, 18 were followed 1 to 3 months (Table II) and 15 cases, 53.5 per cent, asymptomatic and 8 cases (53.6 per cent) improved sufficiently not to require further medication. a total of 23 cases (82.1 per cent). This compared favorably with control groups which varied from 38 per cent to 70 per cent of the cases showing a comparable improvement. Twelve cases, 43.8 per cent showed reversal of previously positive x rays. Control groups of similar cases (best results) showed 20 per cent reversals.

At 6 months to 1 year follow-up patients were asymptomatic and in 6 the results were considered good and at 1 to 3 years only 2 patients remained asymptomatic and 5 were considered to have good results. By this time only 3 x-rays were negative. The course taken by these patients shows the transitory character of the change influenced by hormone administration and the extreme importance of a long careful follow-up in this condition to avoid being misled and making faulty interpretations.

Our only conclusions concerning the daily parenteral injection of estrogen are that it

causes a higher percentage of remission in chronic duodenal ulcer (lasting from 5 to 10 months) than found in controls. Although the number of cases in this group is too small a sample for mathematical calculation, the results seem clear cut. Of greater importance than the subsidence of symptoms (in the clinical course of peptic ulceration) is the healing of the duodenal lesion. This change in pathology occurred (as evidenced by x-rays) in the presence of a markedly increased free and total acidity (Chart 2). It would lead one to doubt the present thought concerning the relationship between the healing of a duodenal ulcer and the lowering of gastric acidity. Others, including Konjetzny who have experimented on an entirely different basis, have come to similar conclusions, at least as far as antacid therapy is concerned (Schiffm and Schindler Necheles and Gold, 65). Although increased gastric acidity may cause erosion in the experimental dog's stomach, when the blood supply to the organ has been severed, this is not the case in unoperated humans, Schindler et al. (65). In our series estrogen raised the gastric acidity in males and in the presence of this raised acidity caused a transitory symptomatic, 82.1 per cent, and in many cases a ray cure of the peptic ulceration, 43.8 per cent.

In 8 cases blood and urine studies for estrogen determination were performed. In all but one the urine estrogen output increased following estrogen administration. Unfortunately simultaneous blood and urine cholesterol and androgen determinations were not made. Since androgen determinations are necessary to gauge the androgen-estrogen ratio and since it is our belief that high urine cholesterol determination may represent an increased hormone excretion, as a result of degradation synthesis of hormones to cholesterol this portion of the work will have to be repeated.

Seven patients had gastroscopic examinations prior to estrogen administration. Since only 2 patients (both of whom showed a normal gastric mucosa despite the increased gastric acidity) had gastroscopic examinations following treatment further evidence of mucosal changes by direct vision is necessary.

this is being gathered and will be presented in separate publication

A case which is not part of our series is of interest in this regard

A 57 year old anemic female complained of epigastric distress, distention, pyrosis, and loss of appetite. Gastrointestinal series showed a deformity of the stomach attributed by the roentgenologist as trophic and hypertrophic gastritis. Suspecting malignancy, this patient was examined by gastroscop and a diagnosis of atrophic gastritis was made. The patient was placed on theelin in oil, 10,000 units twice weekly for 24 injections. Following and during treatment she became asymptomatic and has remained so (19 months follow-up). X-ray examination and gastroscopy of stomach 1 year following treatment were revealed as "no sign of abnormality."

Special attention to endocrinopathies resulting from large doses of estrogens was given. Three patients developed gynecomastia, 2 developed loss of libido. These manifestations lasted from 2 weeks to 2 months following treatment and then completely disappeared. Examination of the prostate and testicles on all patients showed no evidence of change or abnormality. Experience of several observers (Auchincloss and Haagensen and Gemmell and Jeffcoate) has emphasized the inherent dangers in continual hormone injection, especially in large doses. We have no intention of recommending hormone therapy as routine treatment in peptic ulcer and would add our warning to that of others on the possible pathological and carcinogenic activity of these powerful agents. It is possible that, in a patient with a threatening perforation on whom operation was not feasible and in other indicated cases, hormone therapy would be applicable.

Pathological sections on the resected stomachs of the 3 cases which came to operation because of advanced or recurrent peptic ulceration, following a series of estrogen injections, showed that with the exception of the peptic ulcer which had recurred at its original site in the duodenum, the entire gastric mucosa was within normal pathological limits.

Estrogens do not depress the quantity and acidity of gastric secretion. In fact we find, quite to the contrary, that they increased the free and total acidity in those patients who

have been followed up. At present, we know that estrogens have a definite action on the gastric mucosa, whether direct or indirect. Only a small part of the character and extent of such action has been determined.

A similar group of patients to those placed on estrogen therapy is at present receiving male sex hormone, both the number of cases and the length of time they have been studied are insufficient to give any definite results, and the same may be said for the other groups. These will be presented when sufficient time has elapsed.

Although we have several patients receiving gonadotropic hormone (anterior pituitary-like substance), our results are so variable that we are not prepared to report at present. In none of the cases in which these preparations were used was there a consistent change in the character or volume of the gastric secretions, nor in the healing of the ulcerative lesion. It is possible that these results are due to the fact that the dosage given each patient was too little (extracts of low unitage) and this work will have to be repeated.

#### CARCINOGENIC FACTORS INFLUENCING GASTRIC MALIGNANCY

In our recent report (1) of statistical and diagnostic data on cases of carcinoma of the stomach, the discouraging status was emphasized. The magnitude and seriousness of this problem is realized when one is confronted with a condition that accounts for from one-fourth to one-third of the total deaths from carcinoma annually (Livingston and Pack). It is difficult to determine whether the increasing frequency of cancer of the stomach is due to its more accurate recognition. Another factor, the average age at death being postponed so that the patient lives through a cancer age, is more important. The fact that stares us plainly in the face is that the attack rate of gastric malignancy is increasing and accounts for thousands of deaths yearly, and this is the primary reason why new and more successful approaches to this problem are imperative. The disparaging outcome following surgery has been noted, and the need for different approach of this problem is apparent.

TABLE II.—TWENTY-NINE CASES OF DUODENAL PEPTIC ULCER IN MALES TREATED WITH PARENTERAL ESTROGENIC SUBSTANCE (THIELIN)

No.	Age	Years interval prior to ulcer operation	Total number of ulcers operated	Interval prior to ulcer operation	X-ray results immediately before treatment	First 6 months following treatment		6 months to 1 year following treatment		1 year following treatment		1 year following treatment		Further treatment
						Choloid results	X-ray results	Choloid results	X-ray results	Choloid results	X-ray results	Choloid results	X-ray results	
1	38		20	none	+	Asymptomatic	+	Good	+	Good	+	Good	+	
2	44		20	none	+	Asymptomatic	+	Recurrent	+	Recurrent	+	Recurrent	+	Medical
3				none	+	Asymptomatic	—	No data	No data	No data	No data	No data	No data	
4	34		30	none	+	Unimproved	+	Recurrent	+	Good	+	Unimproved	+	12 of 12 (all) in 12 months (none) No data
5	46		none	none	+	Good	+	Asymptomatic	+	Recurrent	+	Asymptomatic Operation	Outfit	Surgical treatment
6	40		none	none	+	Asymptomatic	+	No data	No data	No data	No data	No data	No data	
7	38		none	none	+	Asymptomatic	—	Unimproved	+	Unimproved	+	Unimproved	+	Medical
8	46		10	none	+	Asymptomatic	+	No data	No data	No data	No data	No data	No data	
9	36		30	none	+	Good	+	Recurrent	+	Good	+	Unimproved	+	No additional in 12 months (none) No data
10	46		1000	none	+	Good	—	Good	+	Good	—	Good	+	None
11	34		30	none	+	Unimproved	+	No data	No data	No data	No data	No data	No data	
12	34		15	none	+	Asymptomatic	—	No data	No data	No data	No data	No data	No data	
13	34		71	none	+	Asymptomatic	+	Recurrent	+	Quantitative—good	+			
14	47		71	none	+	Unimproved	+	No data	No data	No data	No data	No data	No data	Medical

1000 = interval in 1000 days; 1000 = interval in 1000 days; 1000 = interval in 1000 days; 1000 = interval in 1000 days.

Unimproved = no change in ulcer; Recurrent = change in ulcer; Asymptomatic = no change in ulcer; Good = no change in ulcer; Quantitative—good = no change in ulcer.

Asymptomatic = no change in ulcer; Good = no change in ulcer; Quantitative—good = no change in ulcer.

Asymptomatic = no change in ulcer; Good = no change in ulcer; Quantitative—good = no change in ulcer.

Asymptomatic = no change in ulcer; Good = no change in ulcer; Quantitative—good = no change in ulcer.

Asymptomatic = no change in ulcer; Good = no change in ulcer; Quantitative—good = no change in ulcer.

TABLE II--TWENTY-NINE CASES OF DUODENAL PEPTIC ULCER IN MALES TREATED WITH PARENTERAL ESTROGENIC SUBSTANCE (THELIN)—Continued

No	Age	Years treated in clinic prior to thelin injection	Total number injections of thelin	International units of thelin per injection	X ray results immediately before thelin treatment	1-3 months following treatment		6 months following treatment		1-3 years following treatment		3-5 years following treatment		Further treatment
						Clinical results	X ray results	Clinical results	X ray results	Clinical results	X ray results	Clinical results	X ray results	
15	33	1	18	10000	+	Asymptomatic	—	Asymptomatic	—	Asymptomatic	—	Asymptomatic	—	None
16	49	2	21	10000	+	Good	+	Good	+	No data	No data	No data	No data	
17	26	1	17	6000	0	Asymptomatic	+	Recurrence	+	Asymptomatic Operation	—	Asymptomatic Gastric	Resection	
18	50	7	18	6000	0	Good	+	Good	+	Good	+	Good	+	Medical
19	43	3	19	10000	0	Unimproved	+	Recurrence	+	Unimproved	+	Recurrence		Medical
20	35	2	24	10000	0	Asymptomatic	+	Unimproved	+	Recurrence	+	No data	No data	Medical
21	37	2	26	10000	0	Asymptomatic	—	No data	No data	No data	No data	No data	No data	
22	29	1	18	10000	0	No data	—	No data	No data	No data	No data	No data	No data	
23	52	2	13	50000	0	Good	+	Unimproved	+	Recurrence	+	No data	No data	
24	47	1	14	50000	0	Asymptomatic	+	Good		Recurrence	+	No data	No data	
25	41	2	14	50000	0	Good	—	Asymptomatic	+	Recurrence	+	No data	No data	
26	36	2	21	10000	0	Asymptomatic	—	Recurrence 5 mos		No data	No data	No data	No data	
7	49	1	21	10000	0	Asymptomatic	±	Asymptomatic	+	Asymptomatic	+	No data	No data	
28	59	2	13	50000	0	Good	±	Good	No data	Recurrence	Hospitalized	No data	No data	
29	44	1	20	10000	0	Asymptomatic	±	Unimproved	+	Recurrence	+	No data	No data	Hospitalized

Note: It should be taken into consideration that upon recurrence of symptoms, oral medication was resumed.

Good: Definitely improved with mild residual gastrointestinal symptoms. No further medication required.

Unimproved: Medication caused no change in gastrointestinal symptoms.

Recurrence of previous severe ulcer symptoms.

No data: Patients did not return for follow up studies.

X ray results: 0 = ulcer present

± = evidence of healed lesion no activity

— = no pathology noted

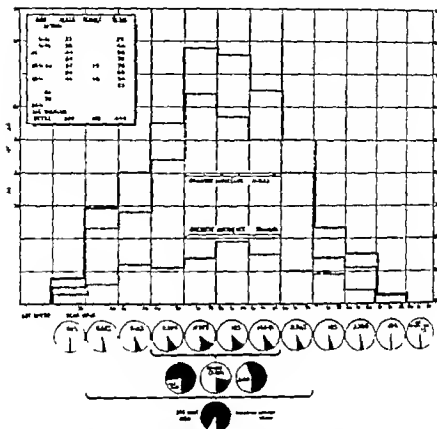


Chart 3. Showing sex and age incidence in gastric carcinoma patients.

Although several claim moderate success Bal four (7) and Gray (27) in the surgical cure of gastric malignancy recent reviews by Boyce Mullen and Oughterson are in agreement with our findings that the outlook in gastric carcinoma in the general population is a very dismal one. A further study by one of us (J. W. H.) comparing selected with unselected cases verifies the finding that the operability and resectability in gastric cancer is definitely influenced by the selection of cases (Saypol and Hinton).

There have been 444 cases of carcinoma of the stomach at the Fourth Medical and Surgical Divisions of Bellevue Hospital during the last 20 years. These cases are charted as to age and sex. The chart is based on consecutive admissions with males and females divided into 5 year groups. The preponderance

of males over females, more than 3 to 1, is conspicuous as illustrated in Chart 3.

Over 88 per cent of the cases fall between the ages of 35 and 70 with the peak of incidence occurring in males between 50 and 55 and females between 55 and 60. The age incidence and sex discrepancy in gastric carcinoma are two facts which stand out in almost every large series reported in recent years (Ballour and Hargis, 8) Minner and Geschickter). It is in an attempt to clarify and explain these two facts that we are presenting information contained in the recent physiological, biochemical, and endocrinological literature.

The carcinogenic effect of estrogenic hormones in the development of abnormal growth and the relationship of sex hormones to tumor formations, have been shown to be both actual

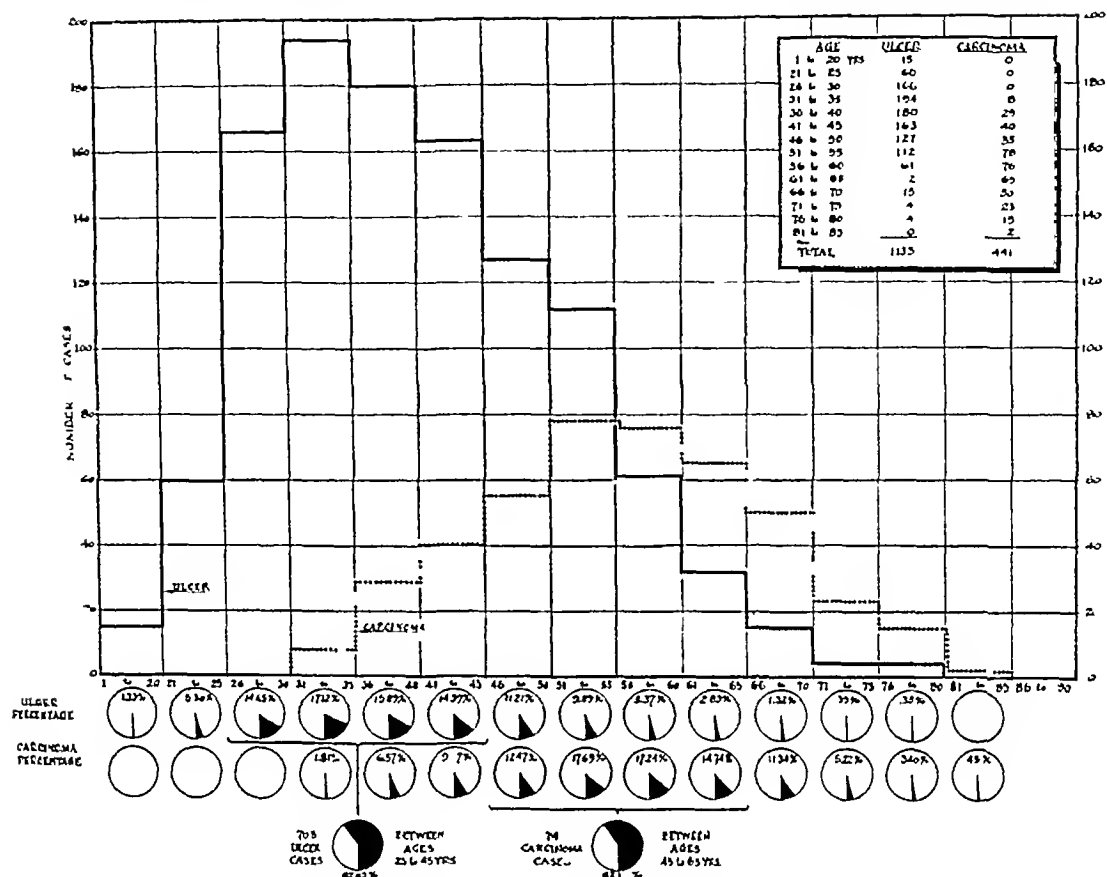


Chart 4 Showing the difference in maximum ages in carcinoma and peptic ulcer

and definite by repeated experiments. Several workers have recovered excess estrogens from the urine of carcinomatous individuals (Aron, Engel, Fiessinger and Moricard, and Saphir). In a review of this subject by Dodds the amount and character of the hormone is discussed and its possible use as a diagnostic and therapeutic aid pointed out. Belief that steroids closely related to androgens and estrogens play an active part in the heightened cellular activity of carcinoma and that their presence is a result of altered pathological anabolism, has been expressed by Murlin and associates, 55

Experiments on the physical reactions of the carcinogenic hydrocarbons with sterols, other than sex hormones, which play an important rôle in human metabolism, have

shown their modes of interchange. Interaction between polycyclic hydrocarbons and sterols and their structural relationship to carcinogenic agents and related substances normally present, into carcinogenic agents within the body has been stressed by Clowes, Davis and Krah, Fieser, and Marker. While the carcinogenic activities of estrogens are supposedly exerted only on the secondary sex organs, Loeb allows that the carcinogenic hydrocarbons have much less specificity of action, and that they may transform any tissue into cancer tissue with which they have continued contact under proper conditions. Findings of increased amounts of normal and abnormal metabolites, compounds steroid in character, in the urine of patients with adrenal tumors and other carcinomas, indicate an

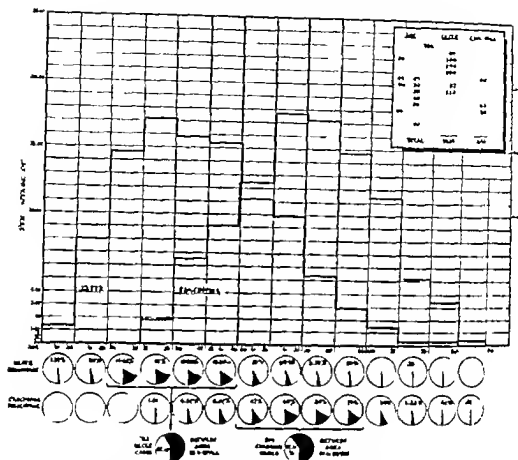


Chart 5. Showing percentage age incidence of peptic ulcer compared with age incidence of gastric carcinoma cases.

increased or altered metabolism of normally occurring substance (Burrows, Cook et al and Murlin Kochakian Spurr and Harvey 55)

Patients with various carcinomas have been found to have a tremendous increase in their urine cholesterol output (Bruger 12). It should be noted that the blood cholesterol, in those cases of carcinoma with increased cholesterol in urine is normal. The increased cholesterol is not associated with increased urine protein. Particularly this finding is not present in epitheliomas of the skin but most notably in visceral carcinoma. This condition is also found in approximately 1 per cent of supposedly normal people against approximately 95 per cent of carcinoma patients (Bruger 13)

Experimental work with the injection of carcinogenic agents into various tissues has shown that tumors develop much more easily in some tissues than others. This finding is applicable to the gastrointestinal tract. A species difference has also been noted. Certain cells within the organism are more susceptible to neoplastic transformation than others under equal contact with carcinogenic agents. However it has also been noted that the response of a given tissue to a carcinogenic agent is specific for both cell and type of carcinogenic agent and has no relationship to spontaneous tumor formation. Rusch, Baumann and Mason injected the subcutaneous layers of the stomach of rats with benzo(a)pyrene in 3 cases and caused the formation of a myxoma, spindle cell

sarcoma, and adenocarcinoma of the stomach. Similar injection in the duodenum did not cause tumor formation.

Stewart, although causing the formation of gastric adenocarcinoma in four mice by the injection of methylcholanthrene into the muscular tissues of the stomach wall, believes that the gastric mucosa is relatively resistant to the action of methylcholanthrene. In this connection the work of Perry and Garton has importance, in that they seem to have broken down the resistance of the mouse stomach to malignancy by combining 1, 2, 5, 6 dibenzanthracene with theelin, thereby causing gastric malignancies which were not caused by the use of 1, 2, 5, 6 dibenzanthracene alone.

Studies of gastric carcinoma in two races living under the same conditions (i.e., Malays and Chinese, have shown the incidence of gastric malignancy to be five times as common in Chinese as in Malays (Snijders and Straub). In an attempt to correlate this discrepancy with the etiology of gastric carcinoma, an accurate study on other racial differences in gastric pathology has been made (Honne, Hart, and associates, 10). Similar racial differences were noted in only 2 other pathological conditions, chronic atrophic gastritis and goblet cell metaplasia, were more prevalent in Chinese. Both of these conditions are common as regressive changes and as potential precursors of carcinoma.

We believe our own statistical and clinical findings agree with animal experiments to indicate that sex hormones affect the gastric mucosa and consequently the incidence of tumor formation. Controversial findings by competent workers are reported, and both estrogens and androgens have been shown to have protective powers against tumors. Estrogens have been reported both as a carcinogenic substance and as an immunizing agent against tumor inoculation and metastases. It would seem that the disproportion between these two hormones and other hormones is of greater importance than the activity of either one. However, since it has been determined that hormone effects are the resultant of the algebraic sum of all the endocrine secretions, we believe that several other hormone effects are involved, namely, pituitary, thyroid, and

adrenal hormones. The tumor forming and the tumor protecting effects of androgens and estrogens are not specific direct effects but general and indirect.

The establishment of atrophic gastritis as a definite disease entity, usually starting at middle life, is a step toward the correlation of gastric physiology and tumor pathology (Schmidler and Murphy, 64). The apparent hormone dysfunction concomitant with this condition and its role in the development of carcinoma lead to a new experimental and therapeutic approach to gastric malignancy (Abrahamson and Hinton, 1; Koch, 30, and Moersch). Koch stated in 1935 that although estrogens are highly carcinogenic substances, they were active only in the tissues in which they induced growth processes. In the past 5 years additional experimental proof shows that several hormones, including we believe the estrogenic hormones, affect the gastric mucosa.

Hormone imbalance or "disbalance" takes place during that period in which neoplastic change most often occurs. Although we realize that there are still many unproved facts to be established, it would seem that this imbalance (a), together with carcinogenic agents normally present (b) plus other predisposing causes (c and d) result in neoplasia of the stomach.

We realize the experimental work mentioned is incomplete, and largely inconclusive. However, the problem of gastric carcinoma is of such tremendous proportions and importance, that we believe many experimental and clinical observations by various workers with sufficient material will be necessary to bring us to a correct conclusion.

#### SUMMARY

1. The clinical, surgical and experimental studies for the early diagnosis and therapy in gastric carcinoma have so far been largely unsuccessful.

2. Two established and unexplained facts are the age incidence and sex discrepancy.

3. The effects of vitamins upon the gastric mucosa as well as elsewhere, are partially due to their relationship with, and effect upon, endocrines.



4 Experimental work shows that the gastric mucosa can be influenced by hormone activity including changes in the androgen-estrogen ratio

5 The possibility of sterols, the sex hormones, and other hormones normally present in the human body being transformed into highly active carcinogenic agents, within the body has been pointed out.

6 Experimental work has shown the relationship of sex hormones to carcinogenic substances and a possible mode of interchange from one to the other

7 Changes in blood contents and activity of several hormones takes place at the time when gastric carcinoma most frequently occurs.

8. We have presented the conception that the gastric mucosa is a gland and therefore, is liable to influence similar to those which control the functioning of other endocrine glands.

9. There are marked differences in blood hormone content between the sexes. Radical changes take place following involution. These differences help explain the sex discrepancy, and age incidence in gastric carcinoma and benign gastroduodenal lesions.

10. We believe that the relationship between the sex hormone control of the gastric mucosa and gastric pathology including neoplasia is an actual one, and that further clinical and experimental work along the principles outlined should be instituted to throw further light on the problems of etiology, diagnosis and therapy of gastric carcinoma.

#### REFERENCES

- ABRAMSON, R. H. and HINTON, J. W. *Surg. Gyn. Obst.* 1940, 7 33
1. ASH, J. C. *rad. Soc. bul.* 1935, 8 58.
2. ASH, J. *Am. J. Obst.* 1940, 879.
3. ATKINSON, A. J. and IVE, A. C. *Am. J. Digest. Dis.* 1935, 3 30
4. ACCONCLORE, H. and H. MOENKE, C. D. *J. Am. M. Ass.* 1940, 4 57
5. BARKER, B. P. *Am. J. Digest. Dis.* 1935, 3 457
6. BALFOUR, D. C. *Am. Surg.* 1937, 3 733-739
7. BALFOUR, D. C. and HANSEN, E. H. *Am. J. M. Sc.* 1937, 71 773
8. BERT and T. YOUNG. *Physiological Basis of Medical Practice* 7th ed. p. 690 Baltimore: Williams & Wilkins Co. 1930
9. BOYCE, C., MARTIN, P. H. et al. *Am. J. Cancer* 1935, 33 264
10. BOYCE, F. F. *J. Am. M. Ass.* 1941, 7 670
11. B. COOK, M. *Am. J. Clin. Path.* 1935, 5 74
12. IDEM. *J. Biol. Chem.* 1935, 103 471
13. BURROWS, H. COOK, J. W. et al. *Biochem. J. Lab.* 1930, 31 970
14. CLOWES, G. H. A., DAVIS, W. W. and KRAUS, W. E. *Am. J. Cancer* 1936, 36 95
15. CULVER, C. U. ATKINSON, A. J. and IVE, A. C. *E. Endocrinology* 1930, 24 63
16. D. J. H. and KOMAROV, S. A. *Am. J. Digest. Dis.* 1930, 6 60
17. DILLON, G. *Atti Soc. Ital. Oncol.* 1931, 35 191
18. DODGE, E. C. *Lancet, Lond.* 1931, 1257
19. EDWARDS, quoted by WAGNER, C. J. *Physiology, Health and Disease* 31 ed. Philadelphia Int. J. Febiger 1930
20. EDWARDS, J. K. *J. Physiol. Lond.* 1905, 31 3134
21. EMMER, D. *Med. Klin., Berl.* 1930, 56 790
22. FERRIS, L. F. *Am. J. Cancer* 1935, 31 37
23. FISHBERG, Y. and MORGAN, R. C. *rad. Soc. bul.* 1934, 1 604
24. FRIEDMAN, M. H. F. *Am. J. Physiol.* 1932, 25 50
25. GIBBS, A. M., and JEFFCOATE, T. C. *J. Clin. Gyn. Brit. Empire*, 1936, 46 475
26. GIL, H. K. *Surg. Gyn. Obst.* 1932, 74 47
27. GIL, J. B. *Am. J. Physiol.* 1937, 30 657
28. GROLLMAN, A. and FINCH, W. M. *J. Natl. M. Ass.* 1932, 50-52
29. HINTON, J. W. *J. Am. M. Ass.* 1932, 98 750
30. HOLLANDER, F. *Proc. Soc. Exp. Biol.* N.Y. 1937, 5 3
31. HUNT, A. *Brit. J. Surg.* 1935, 22 456-461
32. IVE, A. C. *Physiol. Rev.* 1935, 15 211
33. IDEM. *Medicine, Balt.* 1935, 14 5
34. JOHNSON, J. A. *Am. J. Dis. Child.* 1935, 61 75
35. KATZ, A. T. SUMNER, I. et al. *Endocrinol.* 1935, 3 35
36. KLEIN, E. *Arch. Surg.* 1933, 76 33
37. KOCHE, F. C. LECHE, A. B. and KATZ, E. *Am. J. Physiol.* 1930, 32 308
38. KOCHE, H. *Deut. med. Woch.* 1930, 56 1
39. KOPPEL, G. E. *Der Magen Krebs* Leipzig Fehse and Sohn, 1933
40. LEVINTON, E. M., and PAGE, O. T. *End. Results, the Treatment of Gastric Cancer* New York Hoeber 1930
41. LLOYD, L. *Estrogenic hormones and carcinomas* I. *Glandular Physiology and Therapy* 1937 Chicago: American Medical Association, 1937
42. M. WILKIN, I. A. and MURPHY, W. R. *Am. J. Surg.* 1935, 5 45
43. MARINE, D. *Bull. N. York Acad. M. Sci.* 1937, 3 790
44. MARINE, D. and ROBERT, S. H. *J. Mount Sinai Hosp. N. York* 1932, 8 817
45. MARSH, R. E. *J. Am. Chem. Soc.* 1936, 58 171
46. McMillen, J. W. *Radiology* 1941, 37 394
47. MITT, J. H., and LUCKY, R. W. *Illus. M. J.* 1934, 24 46-50
48. MILLER, T. G. and ELSON, K. D. *Radiology* 1941, 37 94
49. MROCK, J. F. and GERSHBERGER, C. F. *Am. J. Cancer* 1937, 7 740
50. MORRIS, R. C. *J. Clin. Endocr.* 1944, 20-21
51. MORRIS, H. J. *Proc. Mayo Clin.* 1939, 14 57
52. M. LLOYD, T. F. *Surg. Gyn. Obst.* 1942, 7 27
53. MURPHY, J. R. *J. Am. Diet. Ass.* 1935, 34 377
54. MURPHY, J. R. *Arch. Path. C. B. Sect.* C. L. vol. 1111 R. A. *Arch. Path. C. B.* 1936, 1 177
55. NIKOLAY, J. T. and MILLER, T. G. *Am. J. Surg.* 1934, 31 89
56. OGDEN, A. W. *Yale J. Biol.* 1932, 4 77

- 8 PERRY, I. H., and GINTON, L. L. Am J Cancer, 1937, 29 680
- 9 RUSCH, H. P., BAUMANN, C. A., and MAISON, G. L. Arch Path, 1940, 29 8
- 10 SANDWEISS, D. J., SALTZSTEIN, H. C., and FARBMAN, A. A. Am. J Digest Dis, 1939, 6 6-12
- 11 SAPHIR, W. Endocrinology, 1934, 18 191
- 12 SAYPOL, G. M., and HINTON, J. W. Am J Surg, 1941, 54 431
- 13 SCHIFFRIN, J. J. Proc Soc Exp Biol, N Y, 1940, 45 592
- 14 SCHINDLER, R., MURPHY, H. M. Am J Digest. Dis 1940, 7 7
- 15 SCHINDLER, R., NECHELES, H., and GOLD, R. Surg Gyn Obst, 1939, 6 281-286
- 16 SHUTE, E. V. J Endocr, Oct, 1940, 2 173-178
- 67 SMITH, G. V., and SMITH, O. W. J Am M Ass, 1931, 97 1857
- 68 SNIJDERS, E. P., and STRAUB, M. Nedl Indië, 1921, 61 624. Tr in Tr Far East. Ass Trop M, 1923
- 69 SPIEGELMAN, ANNA R. Proc Soc Exp Biol, N Y, 1940, 43 307-308
- 70 STEWART, H. L. Arch Path, 1940, 29 153
- 71 STRAUSS, M. B., and CASTLE, W. B. Am. J M Sc, 1932, 184 655
- 72 WELLS, J. A., and GREENE, R. R. Endocrinology, 1939, 25 183
- 73 WEST, P. M., and WIGLON, W. L. Science, 1941, 93 525
- 74 WINKELSTEIN, ASHER. J Mount Sinai Hosp, N York, 1939, 7 29-31
- 75 Idem Am J Digest Dis, 1936, 3 229

# SURGICAL TREATMENT OF PILONIDAL (DERMOID) CYSTS

## A Study of 100 Consecutive Cases of Excision and Primary Closure

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THE subject of pilonidal (dermoid) cysts, with their preoperative preparation, operative treatment, and postoperative management, is a homely but timely one. The true incidence of the disease in civil life is unknown. However at the present time soldiers between the ages of 20 and 25 years are pouring into Army hospitals, requesting attention for infected and draining pilonidal cysts. The problems associated with the management of the lesion in civilian hospital practice are multiple and often aggravating. These same problems, arising in military hospitals coincident with the disease in men assigned to full military duty become formidable.

The primary purpose of an Army General Hospital is the rehabilitation and return of soldiers to military duty as quickly as possible. There is little space available for prolonged hospitalization and no provision for extended convalescence. Therefore, many of the recognized operative procedures in the treatment of pilonidal cysts, such as excision and packing without closure with its attendant delayed healing of from 2 to 6 months must be supplanted. A perplexing complication in this problem, as far as the Army is concerned is the fact that pilonidal cysts are considered to be congenital to have existed prior to induction of the patient into the Army and as such any operative treatment is elective and not an emergency. Furthermore, the economic aspect of the problem must be considered and constantly borne in mind. Most of these soldiers are in the first important phases of their training, having been in the Army only 2 or 3 months. The trauma associated with military training probably activates a hitherto silent lesion, and

some form of treatment must be given. Let that treatment must not entail long and expensive hospitalization, thus depriving the Army and the country of the services of these soldiers.

There are many lesions the surgical treatment of which is elective and may be postponed. However an infected, draining pilonidal cyst requires attention. Soldiers afflicted cannot sit or lie down comfortably, cannot stand without frequent changes of dressing and linen, and experience a decided decline in their military efficiency. Conservative treatment results in improvement which is permanent only so long as no further trauma is encountered. From a military standpoint, these men are greatly handicapped until the lesion is removed.

In view of these facts, the lesion must be removed. But it must be done in such a way that the patient is quickly returned to duty with a healed wound requiring no dressing or care and with as little probability of recurrence of difficulty as possible. Therefore, primary healing of a clean surgical wound following excision of the cyst, is necessary. A routine of preoperative and postoperative management, as well as surgical technique at the time of the excision—the complete excision of the cyst and the primary closure of the wound—has been followed at LaGarde General Hospital with excellent results.

During the 12 months from August 1, 1941 to August 1, 1942 133 patients with pilonidal disease were operated upon at LaGarde General Hospital, New Orleans, Louisiana. This paper is based upon a study of the first 100 consecutive cases. The immediate progress of the 33 remaining patients will be discussed.

### DEFINITION

A pilonidal cyst may be defined as an epithelium lined cavity containing hair fol-

icles, located in the midline, external or posterior to the sacrum and coccyx. Other terms have been applied to the lesion, most frequent of which are pilonidal sinus or fistula, sacrococcygeal dermoid or cyst, postanal dermoid or cyst. Single or multiple epithelium lined cutaneous sinuses may communicate with the cyst, usually opening externally in the midline, but often appearing on the gluteal surfaces at either side.

#### HISTORY AND ETIOLOGY

The condition was apparently first described by J. M. Warren in 1867. He thought it was due to a reversed or ingrowing hair follicle. Hodges probably first used the term pilonidal sinus in 1880, but credited Warren with the first description. Many other theories have been advanced. Mendelstadt (1885) thought the sinus might be derived from the lower end of the spinal cord. About the same time Lannelongue considered that the cyst developed from a process of ectodermal invagination, due to a faulty median skin agglutination of the sacrococcygeal region. More recently Stone suggests that it might be a vestigial structure analogous to the preen gland of birds.

There have been many explanations of the cause of this defect. The most logical is that which holds that the cyst develops as a result of an ectodermal maldevelopment in embryonic life. The cyst probably arises from a failure of complete separation of the primitive medullary canal from true skin. Gage (2) describes this maldevelopment in two ways. First, there is a congenital shortening of the caudal ligament which stretches between the skin and tip of the sacrum. This shortening causes invagination of the skin and, later, as the sacrum proceeds caudalward, a sacral dimple or sinus pointing toward the anus is formed. Second, there is a failure of complete fusion of the two neural folds, leaving a sac, or canal, at the lower end of the spine.

This second type is by far the most common. Gage (2) further divides it into three groups: (1) those confined to the sacrococcygeal region, lying upon and outside the lumbosacral fascia, without entering the sacral hiatus. These are most common. (2) Those

cysts which enter the sacral hiatus but are not attached to the cord. (3) Those rare lesions which not only enter the sacral hiatus but are continuous with the spinal cord.

#### SYMPTOMS AND DIAGNOSIS

The objective findings and symptoms in the disease are so typical that they need little discussion. The true incidence of pilonidal disease is probably unknown, because the cysts when present are congenital and may lie dormant until trauma or undue strain causes drainage or infection. Swelling, pain, and tenderness in the midline, sacral region, should cause suspicion of the presence of a cyst. Often these signs of a low grade infection precede actual drainage. A chronic, dull, lower backache is often present. The recurrence of any of these symptoms, with or without the presence of actual drainage, is typical of pilonidal cyst.

Actual drainage of a thin, whitish material from a midline sinus is pathognomonic of the disease. There may be one or more such sinuses or dimples from which clumps of hair may protrude. Recurrent infection may have caused burrowing subepithelial sinuses and cavities with drainage to the outside through openings lying widely separated in the gluteal regions. Often such cavities and sinuses are so indurated that their course can be palpated. Eighty of these sinuses were draining at the time patients were admitted to hospital, and 20 patients were acutely infected with abscess formation.

Diagnosis should be simple. Tenderness and swelling, inflammation or frank infection in this area should suggest the presence of a pilonidal cyst. Midline openings are pathognomonic. Probes may be inserted in lateral sinuses and will be directed toward the midline. It is rarely necessary to resort to the injection of a radio-opaque substance to prove the presence of the cyst. Such procedure may infrequently be of aid in determining the extent of a lesion. Differential diagnosis is not perplexing. Anal fistulas, presacral dermoids, ischiorectal abscess, carbuncle of the buttocks, syphilis and osteomyelitis of the coccyx or sacrum, may all simulate pilonidal disease.

## TREATMENT

Surgical treatment has offered the best chance of cure. Excision and packing excision and primary closure, or some combination of these two methods have been most frequently used depending upon the individual cases and their needs. Twill has suggested and used radiation therapy in a few cases with excellent results. Bule has used marsupialization of the cyst in selected cases and reports satisfactory results. The open method has been most popular but since the advent of sulfonamides, the closed method has been frequently used.

Wide excision with open packing probably admits of the least chance of recurrence. Kleckner in a series of 4,231 cases reports 1.13 per cent recurrence. The average time of healing is not given, but the usual time in operations such as these is 3 to 6 months. Rogers reports 97 per cent successful excision, with average healing time of 9 weeks. Pickett and Beatty working with 30 cases at the Station Hospital at Fort Sill, Oklahoma, recommend the open method and state the healing time as from 8 to 11 weeks.

General hospitals in the Army could not undertake the excision of pilonidal cysts at the rate of 130 and more a year one every third day. If each case were to remain 3 or 3 months. Yet, excision and primary closure has carried a fearful incidence of infection and recurrence. Kleckner collected 365 cases and they show a recurrence of 23.29 per cent. Swinton and Hodge in 30 cases show 16.6 per cent recurrence. Gage (3) and Strug have each reported relatively large series of cases of excision and primary closure with no recurrences. Plastic types of operation, i.e. the Laher lateral parallel incisions and the pedicle flap modification were not used in this series of 100 cases. Methods utilizing a combination of open and closed technique have not been uniformly successful.

## PREOPERATIVE PREPARATION

Forty per cent of the cases in this series were infected at the time of admission, 20 per cent grossly so. Eighty cases were draining more or less profusely. All had some degree of soreness and drainage. The preoperative treatment is very important. Each patient

was thoroughly shaved and cleaned on admission and this shaving was repeated at least weekly during the hospitalization. The lesions which were infected or draining were intensively compressed with hot saline pack until the evidence of infection disappeared. One or two courses of oral sulfathiazole were given to those grossly infected. A course of treatment was begun with 2 grams of the drug and continued with 1 gram every 6 hours for 3 days, a careful check of the urine and blood being made daily. The diet was not unusual. Mineral oil and milk of magnesia were used daily to insure free bowel movement. Ideally it would have been well to discharge these men with the gross infection as soon as it had resolved and to postpone operation for 2 to 6 months. Obviously this could not be done in the Army. As soon as the acute inflammation subsided, the drainage could practically cease. When the induration and tenderness disappeared, operation was performed on the average of about 1 week later.

Soap-suds enemas were given the night before operation as immediate preoperative measures. Nothing was allowed by mouth after 12 midnight, and a rectal or nebulizer was given the evening before operation as a soporific. Immediately before operation 1/15 grain atropine and 1/4 grain morphine sulphate was given by hypodermic. The entire buttocks and lower back were shaved clean. Methylene blue or other such chemical ferrets were not injected into the sinuses previous to the actual operation. It has been found by Rogers and Hall that such dyes do permeate the walls of the cyst and diffuse through healthy tissue thus necessitating the wider removal of tissue and sacrificing much healthy tissue. The less tissue removed, the less tension will be placed on the wound.

## OPERATIVE PROCEDURE

All these patients were given a spinal anesthetic usually about 75 milligrams of novocain crystals was used. The patient was placed prone upon the table, the pelvis elevated by lowering both head and feet and placing a medium sized sand bag beneath the pelvis. The entire operative area was cleaned thoroughly with soap and water and a dry

sponge was partially inserted into the anus. The scrotum was protected and the area cleansed with ether. An important step in the operation was the placing of wide adhesive straps upon each buttock, about 4 inches on each side of the midline. The tails of these straps were pulled tightly beneath the operating table and fastened. Thus the buttocks were separated, and excellent exposure of the operative field under considerable tension was obtained.

Tincture of merthiolate was applied and the patient was draped, the last tincture of merthiolate sponge covering the rectal sponge. Each sinus and opening was carefully explored with a probe and every indurated tract outlined with the examining finger. The anal region should be carefully observed for possible openings. Methylene blue was injected under pressure into each sinus, and the surrounding tissue compressed forcibly to endeavor to force the dye into every tract.

Since it is extremely important that the skin edges perfectly unite during closure, the incision is started at the anal end of the tract, including the caudalmost sinus. With the scalpel point, the bottommost "V" of the incision is first made. A double elliptical shaped incision is finally obtained, enclosing an average cutaneous area of 5 centimeters by 2 to 3 centimeters. Dissection of the cyst itself is always begun caudally, dissecting from below upward. Often it is necessary to undermine the caudal skin margin, but this cavity may be closed later and is preferable to continuing the incision too close to the anal margin. Care must be taken to avoid injury to the rectum which lies in the bottom of the caudal portion of the wound. The dissection is carried down to the lumbosacral fascia in the midline and the gluteal fascia on both sides. Ordinarily this will include the entire tract. If the tract is entered, the incision is enlarged to contain it. Sinuses projecting laterally may be dissected through incisions perpendicular to the main elliptical incision. Care is taken not to injure the coccyx, and particular care is observed in avoiding laceration of the anal sphincter, with its spectre of fecal incontinence.

A cardinal point in the technique is careful and complete hemostasis. Fine catgut, plain

No 0 or No 00, is used. The patient is asked to strain and cough several times to reveal concealed bleeding points. There should be no possibility of even a small postoperative hematoma. Single sutures of chromic No 2 catgut are placed and held, but not tied, in the base of the wound in such fashion that, when tied, the gluteal fascia on each side will approximate the midline. With the placing of each of these sutures, small bits of the lumbosacral fascia are included to obliterate that dead space. The clamps holding these sutures are pulled upward out of the way. The lower angle of the wound is partially closed before the tension adhesive straps are cut. When the operation is rightly performed, the buttocks fall together, and the view of this angle is obscured. Plain No 1 catgut is placed in the level above the chromic No 2 to obliterate the space at the caudal angle. Usually one or two such sutures may be placed and tied before the tension is released. Two or three end-on mattress everting skin sutures are taken at the lower angle of the wound, with particular care that the opposing skin edges exactly approximate. If there is to be trouble with wound healing in the absence of infection, it will be at this angle, particularly if careful approximation is not obtained. Perspiration, tissue maceration, fecal material and dirt all may be present in this area to defeat healing. Sulfathiazole, or sulfanilamide crystals or powder are plentifully sprinkled in the wound, the adhesive tension strips are cut, and the sandbag is removed from beneath the pelvis. The wound usually falls together with no tension. The previously placed chromic sutures are tied and cut. The wound is closed in layers, No 1 plain catgut and Davis No 24 cotton being used. All dead space particularly must be obliterated, and the skin edges must be carefully approximated. More sulfathiazole powder is sprinkled plentifully in each layer of the wound.

If it has been necessary to excise laterally branching sinuses, these wounds are likewise carefully closed. Particularly careful hemostasis, avoidance of tension, and obliteration of dead space are all-important to the success or failure of the procedure. A pressure dressing is applied, held in place by wide adhesive

straps which are so applied as to draw the buttocks even closer together and remove all possible tension from the wound.

#### POSTOPERATIVE TREATMENT

Almost equally important to the success of the operation, the postoperative management must be carefully planned. The patient remains in bed in any position comfortable to him for at least 5 days and longer in the case of obese patients or those patients who have had previous excisions of the cyst. Liquid diet is allowed the first 24 hours, soft diet the next day or so then a regular diet. No attempt is made to constipate the patient, but neither is he encouraged in any way to have a bowel movement. Most of the patients will have no urge for stool for 6 to 10 days. The first dressing is done the 8th day at which time any sutures which are under tension are cut and the sutures at the lower angle of the wound are removed. Dressings are done sooner upon any indication as continued fever, severe pain, or if a bowel movement occurs. In this latter event, the patient is carefully cleansed and a pressure dressing is reapplied.

An oil retention enema (100 c.c. olive oil) is given the evening of the 9th postoperative day and a small soap-suds enema the morning of the 9th day after operation. Mineral oil, 1 to 2 ounces, is also started the evening of the 9th day. All sutures are removed on the 10th postoperative day.

Chemotherapy after operation is rarely used. In those cases in which a rather severe infection had been present before operation and if inadvertently the cyst was entered at operation prophylactic doses of sulfathiazole are given. There have been no untoward effects from the prolonged period of constipation after operation. There have been no fecal impactions. Likewise, there has been no separation of wounds through the strain of defecation too soon after operation, and the incidence of wound infection is greatly lessened.

#### RESULTS

One hundred and thirty-three patients were treated as described at LaGarde General

Hospital. The first consecutive 100 were studied, since most of those patients had been discharged 6 months and more. As readily stated, in 40 per cent of these cases there was some degree of infection at admission, and 80 were draining when first seen. Thirty-eight had had previous incision and drainage of the lesion, 10 had had more than one such temporary surgical relief. Ten per cent of these cases were recurrent pilonidal cysts, and according to the histories obtained from the patients, in 3 of these 10 recurrent patients had had the open type operation, 67 remaining had been closed primarily. The histories are entirely unreliable, however, as far as the type of operation previously performed is concerned. Four of the patients had had more than one operation performed in an effort to eradicate the disease.

While the number of draining sinuses is an index to the severity of the lesion, it is interesting to note that over 90 per cent (93) of these patients had two or more patent sinuses. The average age of the patients was 23 years. There was one colored patient in the series. The average duration of symptoms was 3 and 2/5 years, but nearly one-third (31 per cent) had had no symptoms referable to the lesion until they had been inducted into the Army and were subjected to the trauma associated with military training.

Of the 100 cases under study 98 were entirely successful. There were 2 patients who returned with typical recurrent pilonidal cysts. One had had a very large cyst necessitating a modified Lahey type of closure and had been operated on once previous to the attempt at LaGarde General Hospital. The other demonstrated the necessity for scrutinizing carefully the midline approaching the anus. A small opening near the anus led directly into an epithelium lined sinus which in turn communicated with the recurrent cavity. Both these patients had had mild postoperative wound infections the second undoubtedly because of the anal sinus.

The average time until complete healing in the usual, uncomplicated case is 14 days. These patients are dismissed to full duty on the 22d or 23d postoperative day with well healed soft wounds. The most usual com-

ication, and the one which causes the greatest delay in healing, is infection. There were five moderately severe and two severe wound infections. In all of these a large hematoma was first evacuated, demonstrating the need for meticulous hemostasis. Five definitely were closed with more than the usual amount of tension on the wound. Two of these patients had a mild diarrhea the 3d and 4th postoperative days, and it is conceivable that either the straining at defecation or soiling because of defecation contributed to the infection. Several mild infections of the "stitch-sciss" type were present, but cleared spontaneously.

The delay occasioned by these infections caused the average time of discharge to duty to be elevated to 28 days. Considering the series as a whole, these results are very encouraging. When it is further remembered that 72 of these cases returned to duty in about 3 weeks, the management suggested gains merit. Of the 72 cases remaining in the hospital 25 days or less, 5 cases had had recurrent lesions, and 20 had had previous incision and drainage of an acutely infected lesion. Of the 28 cases remaining hospitalized 25 days or more, 1 case had had multiple previous operations, 18 had had previous incision and drainage either once or more often.

Other postoperative complications were rare. Only one patient developed signs of renal insufficiency as evidenced by a relative anuria and multiple casts in the urine. Chemotherapy was stopped, fluids orally and parenterally forced, and the patient responded quickly.

#### EVALUATION

In the treatment of infected and draining pilonidal cysts in soldiers, the primary and most important objective is to excise the lesion surgically, and return the men to military duty as quickly as possible with a soft, healed wound. There is no single factor which contributes most to successful completion of this task. The entire rationale of treatment is important. The infected cysts must be treated conservatively until the acute inflammation has subsided.

In the operative treatment of these patients, the three cardinal principles of surgical pro-

cedure anywhere must be followed meticulously: (1) Hemostasis must be absolutely complete, (2) tension upon the wound edges must be at a minimum, and this is accomplished by adequate exposure and care to remove only as much tissue as absolutely necessary. It has been found that blocks of tissue 5 by 3 by 3 centimeters usually suffice to enclose the cyst entirely, (3) there must be no dead space remaining when the wound is properly closed.

Completely satisfactory eversion and approximation of the skin edges will aid greatly in complete healing of the wound. All such wounds are soft and nontender, and certain procedures recommended to forestall painful cicatrix are unnecessary. As in all surgical procedures adequate exposure is necessary, and the method suggested is satisfactory. The use of sulfonamide powders in the wound and orally, before and after operation, probably has been a great factor in reduction of the incidence of wound infection. Such infections, when developed, are best treated by adequate drainage and conservative treatment with daily hot sitz baths or compresses. The areas must be kept shaved completely.

Postoperative treatment is directed toward prevention of any undue tension upon the wound, and protection as carefully as possible against infection. Bowel movements are not encouraged until the 9th postoperative day, dressings are not changed unless necessary before the 7th postoperative day, and the wounds are never probed. The patients are kept in the hospital until their discharge and are not allowed the usual freedom of passes because of the possibility of traumatizing the wound inadvertently.

#### SUMMARY

1 One hundred consecutive cases of pilonidal disease in which patients were treated surgically by excision and primary closure were studied. Eighty per cent of the patients had draining sinuses upon admission. Ten patients had had previous operations, in which some type of excision had been done, 38 had had previous incision and drainage.

2 A program of preoperative treatment, surgical technique of excision with primary



closure and postoperative management of pilonidal cysts in the Army Hospital has been described.

3. An incidence of recurrence of 2 per cent is reported. The wounds healed in an average of 21.5 days, the patients were returned to full military duty in an average of 28 days.

4. Seventy two per cent of the patients had completely healed wounds in 14 days, and were hospitalized less than 25 days, returning to duty rehabilitated as useful soldiers.

5. Aside from the suggested preoperative and postoperative management 5 factors are responsible for these results: (a) completely meticulous hemostasis (b) avoidance of tension in closure (c) obliteration of all dead space knowledge of the anatomy of the region and care to avoid damage to the coccyx and anal sphincter (d) the liberal use of chemo-

therapy locally and generally (e) careful approximation of wound depths and edges.

#### REFERENCES

- Butt, L. A. *Practical Proctology*. Chapter 15. Philadelphia & London: Saunders & Co. 1917
1. GAGE, M. *Internat. Clin.* 1936, 3: 19.
2. *Ibid.* *Ann. Surg.* 1936, 100: 201.
3. HODDER. Quoted by Stone, H. B. *Loc. cit.*
4. KLUFTONER, M. T. *Am. Pract. Sec.* 1934, 17: 10.
5. LAVOGLIO. Quoted by Pickett, W. J. and Beatty, A. J. *Loc. cit.*
6. MICHIELSTADT. Quoted by Stone, H. B. *Loc. cit.*
7. PICKETT, W. J. and BEATTY, A. J. *Am. J. Surg.* 1942, 55: 375.
8. ROGERS, HORATIO. *N. England J. M.*, 1930, 101.
9. STONE, H. B. *Ann. Surg.* 1934, 79: 419.
10. STONE. Quoted by GAGE, M. *Loc. cit.* (3).
11. SWIFTON, A. W. and HODDER, C. C. *Surg. Clin. N. America*, 1930, 9: 600.
12. TELL, ROBERT. *Surgery*, 1930, 8: 449.
13. WARRER, J. M. Quoted by Pickett, W. J. and Beatty, A. J. *Butt, L. A. and Stone, H. B. Loc. cit.*

# THE SURGICAL TREATMENT OF INFANTILE HYDROCEPHALUS

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THERE is widespread pessimism in regard to the treatment of hydrocephalus. Thus Bucy remarks "Except for cases that cure themselves, i.e., those that undergo spontaneous arrest, the outlook is almost hopeless. The majority die within the first four years of life, the first year claiming most of them. At the present time, even the best-intentioned surgery can hardly serve other than to deny to some few cases the possibility of a spontaneous recovery by subjecting them to an operation and a surgical death."

So thoroughly convinced of the hopelessness of the situation are many physicians that cases of the relatively benign (Ingraham, 14), "external hydrocephalus" (subdural hygroma) go unrecognized for want of a puncture of the fontanelle, and any suggestion of increase of pressure of the spinal fluid is often considered a contraindication to operation on a meningocele (19). Yet by now, in a number of cases of hydrocephalus patients have been followed for years after successful operations of various types (Dandy, 4, 5, Putnam, 21, 22, 23, Scarff, 25, 26), and at least 2 series of cases are on record (23, 26) in which the operative mortality is low, and a large proportion of survivors are growing up in normal health.

The purpose of this paper is to describe the author's present technique, as it has evolved over 7 years, and to give a statistical report of his series, including a follow-up on some of the original cases (23). Recent reviews of the results of similar operations have been given by Scarff (26) and Dandy (5).

## THE NATURE AND MECHANISM OF INFANTILE HYDROCEPHALUS

The term hydrocephalus is currently used to denote several distinct entities. A collection

of fluid between dura and arachnoid is often referred to as an "external" hydrocephalus. In most instances, such fluid is high in protein and represents the residual of a subdural hematoma. An abnormal amount of subarachnoid fluid is sometimes spoken of as hydrocephalus, the collection is due to atrophy of the convolutions or irritation of the meninges. Atrophy of the brain as a whole gives rise to a dilatation of ventricles with normal intracranial pressure and has been called hydrocephalus. The use of the term "hydrocephalus" for these conditions is misleading, is not in accord with the classical description<sup>1</sup>, and should be abandoned.

Entirely distinct from these entities, is the enlargement of the ventricles due to a chronic increase of pressure within them (23). The increase in pressure may in turn be due to any one of a variety of causes. It may result from an excessive secretion of fluid, from a papilloma of the choroid plexus, or from a hemangioma of the ventricular wall. Or it may result from a block of the aqueduct by an atresia, or of the fourth ventricle by means of a tumor. All of these sources of excessive pressure are rare in infants, and they will not be considered in this paper.

The common cause of chronic increased intracranial pressure is a peculiar congenital defect, of which the mechanism is still obscure. There is no reason to believe that the choroid plexus produces an excess of fluid in such cases, for the aqueduct may also be dilated. The foramina of Luschka and Magendie may or may not be atretic, or drawn down into the foramen magnum by an Arnold-Chiari deformity (3). There is some evidence that the

<sup>1</sup>The condition of infantile hydrocephalus was doubtless known to the ancient Greeks. As far as I can find, it was not mentioned by Hippocrates. In spite of the reference to his works given by Richard Whytt, whose oft-cited description is overrated. The earliest description I have been able to find is that of Celsus, who says "Ubi humor cutem inflat, eaque intumescit et prementis digito cedit υδροκεφαλον, Graeci appellant." Apparently there fore the earliest authors recognized abnormal pressure as the fundamental characteristic of the disorder.

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closure and postoperative management of pilonidal cysts in the Army Hospital has been described.

3 An incidence of recurrence of 2 per cent is reported. The wounds healed in an average of 21.5 days, the patients were returned to full military duty in an average of 28 days.

4 Seventy two per cent of the patients had completely healed wounds in 14 days, and were hospitalized less than 25 days, returning to duty rehabilitated as useful soldiers.

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therapy locally and generally (e) and approximation of wound depths and edges.

#### REFERENCES

1. BOTA, L. C. Practical Proctology. Chapter 11. Philadelphia & London: Saunders & Co. 1931.
2. GAER, M. Internat. Clin. 236, 3 19.
3. Idem. Ann. Surg. 930, 100 20.
4. HODGES. Quoted by Stone, H. Loc. cit.
5. KLECHNER, M. T. Am. Proct. Soc. 1934, 177.
6. LAVOGLIO. Quoted by Pickett, W. J. and Beatty A. J. Loc. cit.
7. MICKELSTADT. Quoted by Stone, H. B. Loc. cit.
8. PICKETT, W. J. and BEATTY A. J. Am. J. 57, 943, 95 375.
9. RODGER, HOR. THO. N. England J. M. 1940, 21 2.
10. STONE, H. B. Ann. Surg. 922, 79 170.
11. STONE. Quoted by Gage, M. Loc. cit. (j).
12. SEXTON, N. W. and HODGES, C. C. Surg. Clin. S. America, 930, 9 600.
13. TWILL, ROBERT. Surgery, 920, 2, 469.
14. WARRER, J. M. Quoted by Pickett, W. J. and Beatty A. J. Bone, L. A. and Stone H. B. Loc. cit.

# THE SURGICAL TREATMENT OF INFANTILE HYDROCEPHALUS

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INFANTILE is widespreadly recognized in regard to the treatment of hydrocephalus. Thus Buerger remarks: "Except for cases that cure themselves, the outlook is almost hopeless." The prognosis due within the first six months of life, the first year, and the first five years, is not of the same. At the present time, even before the advent of surgery, can hardly be other than to die, to some few cases the possibility of a spontaneous recovery by subjecting them to an operation and a surgical death.

So the mortality can indeed be the hopeless, as in the situation are in any physicians that cases of the relatively benign (Ingraham, 11) external hydrocephalus (subdural hydrops) are recognized for a part of a puncture of the fontanelle, and any suggestion of increase of pressure of the spinal fluid is often considered a contraindication to operation or a meningococci (10). Yet by now, in a number of cases of hydrocephalus patients have been followed for years after successful operations of various types (Dandy, 4, 5; Putnam, 21, 22, 23; Scarff, 25, 26) and at least 2,000 cases of cases are on record (25, 26) in which the operative mortality is low, and a large proportion of survivors are growing up in normal health.

The purpose of this paper is to describe the author's present technique as it has evolved over 7 years, and to give a statistical report of his series, including a follow-up on some of the original cases (23). Recent reviews of the results of similar operations have been given by Scarff (26) and Dandy (5).

## THE NATURE AND MECHANISM OF INFANTILE HYDROCEPHALUS

The term hydrocephalus is currently used to denote several distinct entities. A collection

of fluid between dura and arachnoid is often referred to as an "external" hydrocephalus. In most instances, such fluid is high in protein and represents the residual of a subdural hematoma. An abnormal amount of subarachnoid fluid is sometimes spoken of as hydrocephalus; the collection is due to atrophy of the convolutions or irritation of the meninges. Atrophy of the brain as a whole gives rise to a dilatation of ventricles with normal intracranial pressure and has been called hydrocephalus. The use of the term "hydrocephalus" for these conditions is misleading, is not in accord with the classical description, and should be abandoned.

Entirely distinct from these entities is the enlargement of the ventricles due to a chronic increase of pressure within them (24). The increase in pressure may in turn be due to any one of a variety of causes. It may result from an excessive secretion of fluid from a papilloma of the choroid plexus, or from a hemangioma of the ventricular wall. Or it may result from a block of the aqueduct by an atresia, or of the fourth ventricle by means of a tumor. All of these sources of excessive pressure are rare in infants, and they will not be considered in this paper.

The common cause of chronic increased intracranial pressure is a peculiar congenital defect of which the mechanism is still obscure.

There is no reason to believe that the choroid plexus produces an excess of fluid in such cases, for the aqueduct may also be dilated. The foramina of Luschka and Magendie may or may not be atretic, or drawn down into the foramen magnum by an Arnold-Chiari deformity (3). There is some evidence that the

The etiology of infantile hydrocephalus was doubtless known to the ancient Greeks. As far as I can find, it was not mentioned by Hippocrates. In spite of the reference to his works given by Richard Whitt, whose oft-cited description is overrated. The earliest description I have been able to find is that of Celsus, who says: "Cibi humoresque in ventriculis et intestinis et prementibus duntaxat. Cerebrum graecis appellatur." Apparently therefore, the earliest authors recognized abnormal pressure as the fundamental characteristic of the disorder.

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arachnoid is obstructed about the cerebellum or over the convexity in many cases. There is a normal, or almost normal transmission of dyes and of pressure relationships between ventricles and lumbar sac. Whatever the mechanism the pressure is often elevated to a degree to endanger the brain—sometimes as high as 400 millimeters of water over long periods of time.

The obstruction to the flow of fluid is usually not the only abnormality present, however. It is often associated with a meningocele and may become manifest only when the sac is repaired. In such instances, the Arnold Chiari malformation is usually present (24). There may be instead, or in addition, severe cortical aplasia, agyria, microgyria, absence of the corpus callosum, or a miscellany of other serious defects (22-24).

#### INCIDENCE AND RESULTS OF HYDROCEPHALUS

According to Murphy hydrocephalus alone or with spina bifida was reported in 88 living children among approximately 150,000 births. An even higher incidence has been reported by other observers (27). This figure obviously fails to include the surgically important cases which appear later in infancy or following operation on a meningocele—perhaps numbering as many again.

There are no statistics to show the mortality from hydrocephalus alone or from associated deformities. The death rate is certainly high. Occasional infants are said to recover with nonoperative treatment and without damage to the brain. Thus, Penfield (19) states: "Postural dehydration is a method of treatment for mild cases." For 10 years I have used this treatment for less severe cases—and I have seen many (perhaps 10 or 12) permanent cures particularly in cases associated with spina bifida. This the author has never observed and no other statistics are available. The actual cases reported by Penfield are not particularly encouraging (20). It is possible that some of the cases to recover were instances of a temporary osmotic or inflammatory excess of choroid secretion.

Certain infants suffering from hydrocephalus survive to adult life although they cannot

be said to recover. Most of them are well minded, but in a few instances, normal mental development is attained in spite of gross enlargement of the head (23). It has been supposed that a mild hydrocephalus is favorable to outstanding mental development. A survey of the autopsy records of the distinguished men usually selected as examples (Cuvier, Helmholtz, Gauss, Menzel) leads to support to such an idea. It appears that none of them suffered from true hydrocephalus as here defined.

#### DIAGNOSIS AND PROGNOSIS IN INDIVIDUAL CASES

The following outline of procedure is suggested on the basis of the author's experience. It has evolved gradually during the growth of the series of cases presented but in general represents the routine usually followed for the cases in the "new series," which will be presented subsequently. Nothing is to be gained by any radical treatment of cases of hydrocephalus in which the head is enormous at birth, or other obvious external defects exist.

The symptoms which usually first give rise to a suspicion of the existence of hydrocephalus are a slight enlargement of the head or persistence of fullness of the fontanelle when the head is elevated. This may come on spontaneously at any time within 6 months after birth, or after operation for meningocele. The child becomes dull or fussy, feeds poorly, and vomits. Two questions then present themselves. The first is: what is the origin of the increased intracranial pressure? The second is: what is the outlook for the child's mentality if the pressure is relieved?

The question as to the type of hydrocephalus present is ordinarily easily answered if the condition arose following an operation for meningocele. If it came on spontaneously the problem is sometimes settled by an x-ray of the skull which shows not only separation of sutures but also a fenestration of the bone in many cases of congenital hydrocephalus (Fig. 1).

Further information may be obtained by puncture through the anterior fontanelle. This should be performed with the patient in a recumbent position. If the baby is placid, a

curate pressure measurements may often be obtained without the use of an anesthetic, if there is any difficulty, however, the subcutaneous administration of evipal or pentothal is advisable. The normal infant should have an intracranial pressure of 50 to 80 millimeters of water (measured from the scalp). If the pressure is normal or nearly so, operation may be safely postponed.

Aside from measurement of pressure, it is of great importance to measure exactly the depth at which fluid is obtained. The scalp and skull are less than 0.5 centimeter in thickness. If fluid is obtained at this depth, it is probably subdural in origin. Arachnoid fluid is practically never obtained. The depth beyond the dura is a measure of the thickness of the ventricular wall, which is naturally of prognostic importance.

The fluid should be examined for cells, and a determination of protein, sugar, and gold sol should always be made. Meningitis in infants—apparently especially in premature infants—may exist with relatively little effect on the general condition or temperature, and is easily mistaken for congenital hydrocephalus. The presence of blood or a xanthochromic fluid or a protein content of 100 milligrams or more, usually means a subdural hygroma. The recognition and treatment of this common condition is extremely important (14), but it will not be considered further here.

Usually no other special examinations are needed for diagnosis. Ventriculography in hydrocephalic infants carries such a high mortality—almost half that of endoscopy—that it should be avoided if possible. In puzzling cases it may be of great value, and by its use Scarff (26) has been able to demonstrate a growth in thickness of the cortex after operation. Injection of dye into the ventricles is seldom of decisive value. If the results of other examinations are inconclusive or apparently contradictory, one or the other of these procedures may be carried out, but they are seldom essential.

In cases of atresia of the aqueduct, hydrocephalus is usually either present at birth, or develops suddenly with high pressure. Obstruction of the fourth ventricle by tumor also produces an acute hydrocephalus, but seldom

early in infancy. If either is suspected, simultaneous ventricular and lumbar puncture should be performed (under a soporific), and the degree of dynamic block demonstrated. Comparison of the protein content of the fluid in the two ventricles and in the lumbar sac is also sometimes helpful in diagnosis. In case there is still doubt, air may be injected into the ventricles.

Quite as important as the neurological diagnosis is an estimate of the infant's mental activity. Hydrocephalic babies who feed poorly, take no interest in their surroundings, and do not cry or respond, are presumably the victims of extensive cerebral defects or irreversible damage to the brain, and should seldom be operated upon. They practically always die whether the pressure is relieved or not. If there is any question whether the symptoms are due to pressure alone, daily ventricular punctures may be done to see if improvement occurs.

More difficult is to judge how near normal a somewhat responsive child is. The mother's estimate is rarely to be trusted. An experienced psychometrist or child psychologist is often of great help in deciding. If none is available, a careful inventory should be made of all the child's activities—reaching for objects, fixing and co-ordinating the eyes, evidence of recognition of mother or nurse, spitting unpleasant objects (paper soaked in vinegar) out of the mouth, repeating syllables.

There are several brief tests which describe tests suitable for determining the degree of development of young infants. The *Iowa test scale for young infants* (13) is inexpensive and easily obtainable. A more extensive treatise is *Testing Children's Development from Birth to School Age* by Buehler and Hetzer. The tests described by Kuhlmann are simple and reasonably reliable.

While the surgeon should always insist on a psychometric examination being carried out, for his own protection, it must be admitted that circumstances often arise which make it difficult for him to refuse operation, even when the mentality is questionable. He should, however, at least give the patients and the referring physician due warning that the prognosis is poor.

#### NONOPERATIVE TREATMENT OF HYDROCEPHALUS

Several nonoperative forms of treatment have been suggested: the administration of diuretics (16) irradiation of the choroid (18) and postural drainage keeping the infant propped in a sitting position (19). Statistically valid series of case reports, giving pressures or head measurements before and after such forms of treatment, have not been published. In favorable cases, in which the infant's mental activity approaches the normal and there are no definite contraindications to operation, conservative methods of treatment should not be used for more than 2 or 3 weeks if the intracranial pressure is above 150. If it is above 300 a moderate emergency exists, and operation should be undertaken at once.

#### DESTRUCTION OF THE CHOROID PLEXUS IN THE TREATMENT OF HYDROCEPHALUS

This is the only form of treatment which will be considered here. The papers of Davidoff and D'Errico discuss the other types.

Endoscopic coagulation of the choroid plexus was first successfully carried out by Lescapart in 1910 by means of an operating cystoscope according to Davis. It has been sporadically utilized since. The whole subject was put on a sound physiological basis for the first time by Dandy and Blackfan in 1918 (8). Dandy later (6, 7) proposed destruction of the choroid plexus by an open operation, the present form of which was first announced in 1928. The procedure consists of inserting a speculum (Kelly cystoscope) through the cortex emptying the ventricle and removing the choroid after clipping its ends. Both sides are done at one sitting.

Stimulated by Dandy's work and by the use of an endoscope for viewing the anterior of the ventricle by Fay and Grant and by Mixer in 1921, Scarff (15) and the author (11) almost simultaneously but independently designed special endoscopic instruments for the coagulation of the choroid plexus.

#### TECHNIQUE OF ENDOSCOPIC COAGULATION OF THE PLEXUS

The glass bipolar ventriculoscope is recommended for the following reasons. There is

practically no space wasted in the construction; all of it except the electrodes is devoted to the transmission of the image. This large optical aperture permits far clearer vision in a cloudy medium than do instruments of the cystoscope type. The diameter of the instrument is smaller than that of any other operating endoscope. It has a deep focus; structures in the ventricle may be seen at a distance of several centimeters, or in direct apposition. Nothing projects outside of the field of vision. Most important of all, the current passes only between two closely placed electrodes actually in the field of vision, and is therefore confined to structures floating in the fluid. When unipolar coagulation is used the current necessarily passes through the basal nuclei, often producing softenings (12).

The glass ventriculoscope has certain disadvantages. There is some difficulty in obtaining proper glass and in grinding it to exactly the correct form. Some of the earlier instruments especially were unsatisfactory in one or the other respect. It is fragile. The front surface is easily scratched or pitted by permitting sparks to pass between the electrodes through the air. The electrodes are easily torn out. The instrument cannot be boiled or autoclaved, but must be sterilized by immersion in 70 per cent alcohol.

#### TECHNIQUE OF OPERATION

Inhalation anesthetics are to be avoided. Tribromethanol by rectum, sodium pentobarbital by mouth, or one of the soluble barbiturates subcutaneously are satisfactory. Anesthesia may be supplemented by minute doses of morphine.

When the infant is immobilized, the entire head is shaved. (This is a favorable opportunity to take a photograph.) The patient is placed on an elbow high table with a folded blanket under the right hip and shoulder and the head turned as far to the left as it will go. The head is elevated on sandbags, and kept in this rotated position so that the site of proposed incision is approximately uppermost (Fig. 2). A scrub with alcohol followed by bichloride is an efficient preparation.

The incision should be a curved one, about 5 centimeters long to give access to a spot

centimeters from midline in the parieto-occipital region, well away from the motor cortex. The skin is infiltrated with procaine, and the area of incision outlined with a scalpel. Draperies are applied—a mastoid sheet is excellent for the purpose. The incision is then carried cleanly through skin and periosteum in one sweep. Few hemostats are required to check bleeding. A self-retaining retractor is inserted.

The bone is perforated with a hand-drill or a small periosteal elevator. It is removed to expose an oval area of cortex about 2 by 3 centimeters in size. Before the dura is opened, the pressure in the ventricle should be measured by means of a manometer attached to a needle, if this has not already been done. The dura is then opened by a straight incision, and any large vessels in the underlying pia are clipped or stitched to it. An incision about 2 centimeters long is made through the pia, and extended into the ventricle with the handle of a scalpel.

At this point, the operator puts on a sterile celluloid mask, extending over the mouth and nose, which might occasionally touch the top of the instrument. The operating room is completely darkened. The instrument, with wires attached to the lamp battery and to the diathermy apparatus, is carefully inspected to make sure that both ends are clean. The lamp carrier is retracted within the instrument, which is then plunged into the ventricle. As soon as the tip is in fluid, the lamp carrier is cautiously pushed forward until adequate illumination is secured.

The difficult part of the operation consists in locating and destroying the plexus without injuring the walls of the ventricle. This is accomplished by moving very slowly down the septum pellucidum, and following a vein from its smaller tributaries to its termination adjacent to the plexus. The instrument should be rotated so as to keep the point of the lamp away from the wall. When the fluffy pink plexus is encountered, the tip of the instrument is placed directly upon it. A coagulating current, barely strong enough to cause a change of color of the tissues and never permitted to spark, is passed for about a second for each area touched. The plexus is followed first on its lateral surface, well into the anter-

ior horn, over the glomus, and as far as possible into the temporal horn. Particular care should be taken to move the glomus about and turn it over, for it often lies in folds.

During the course of coagulation, the front surface of the instrument tends to become covered with precipitate, and it must often be removed for cleaning. Relatively little bleeding may seriously obscure visibility, which, however, usually improves as time goes on. Some of the blood may be washed out by syringing with large volumes of Ringer's solution. Bleeding points should be sought and coagulated thoroughly. Care should be taken not to get air into the ventricle or under the dura. It should also be remembered that any bubbles given off during coagulation are a mixture of hydrogen and oxygen, and therefore explosive.

Sometimes there is a perforation of the septum, and it is possible to reach the contralateral choroid plexus. Usually, however, it is best to content oneself with a thorough destruction of one side at a sitting, as this is less of a strain on the patient than a bilateral operation.

When the plexus is thoroughly coagulated—which ordinarily takes 20 to 50 minutes—the instrument is withdrawn. The dura is carefully sutured. It is desirable to sew the periosteum in the layer of sutures in the galea. The skin is closed separately. A small collodion or latex cocoon is the only dressing required.

A transfusion or infusion is desirable, and the child can then be returned to its usual schedule as soon as it recovers from the anesthetic.

No particular after-care is needed. Feeding may be difficult for a few days. If the fontanelle remains tense, it may be punctured to remove fluid, which is then usually found blood-stained. As soon as the fluid becomes clear, or within 2 weeks, the advisability of operating on the opposite side may be considered. If there is any real doubt about it, reoperation is best postponed until it becomes clearly necessary.

Occasionally reoperation also fails to give adequate relief. If this occurs, the first operative wound or both should be re-opened and the plexuses inspected to see if any tags of secreting tissue are left behind.



TABLE 1.—INFANTILE HYDROCEPHALUS TREATED BY ENDOSCOPIC COAGULATION OF THE CHOROID PLEXUSES

	Old series 1934	New series 1935-1945
Patients	7	5
Operations	36	35
Hospital deaths	2	4
Later deaths	2	7
Survivors		14

RESULTS OF TREATMENT OF INFANTILE HYDROCEPHALUS BY ENDOSCOPIC COAGULATION OF THE CHOROID PLEXUSES

One of the two patients operated upon by Lespinasse survived the operation and lived 5 years according to Davis.

It is a pity that Dandy's cases have not been reported in detail. Although his method differs fundamentally from the one outlined here inasmuch as a large opening is made in the brain and the ventricular fluid is removed, his statistics would be of great interest. Writing in 1932 he states "Although the author has suggested removal of the choroid plexus from both lateral ventricles for this type of hydrocephalus, the survival period has not been long enough to be certain of cures" (4).

In a later article (1938) Dandy states "I have had several undoubted cures resulting from this method," and reports 2 cases (5). He suggests that removal of the choroid plexus in the fourth ventricle be carried out if removal of the glomus is insufficient. As a last resort, he suggests resecting the plexus in the body of each lateral ventricle—a procedure which is usually carried out routinely as a part of endoscopic coagulation.

Scarff's results have been recently presented in detail (26). He has performed 43 operations on 20 patients, with 3 operative deaths. In 7 other cases, the symptoms were not relieved and the patients died within a few months.

Of the survivors of the operation 1 died of pneumonia 5 years after the operation. In another the pressure has not been satisfactorily relieved. Four of the survivors are apparently normal mentally according to careful psychometric tests. The interval since operation in the group of normal cases has been 8 months to 4 years. Of particular interest is the fact that Scarff was able to demonstrate an actual increase in the thickness of the

ventricular wall after operation, by a comparison of preoperative and postoperative encephalograms.

RESULTS IN THE AUTHOR'S CASES

The author's cases of infantile hydrocephalus have been arbitrarily divided into two groups. The first series includes all of the patients operated upon during the developmental period of the operation, at the Children's Hospital Boston. During this period cases were taken without selection, and none were included in which such conditions as leaking meningoceles, gross abnormalities of the brain, prematurity etc., complicated the picture of increased intracranial pressure. Certain rules of thumb embodied in the directions for study and operation which have just been given were derived from these experiences and have undergone slight evolution since. The second series includes all of the patients subsequently operated upon (chiefly at the Boston City Hospital and the Neurological Institute of New York).

The statistics of the "first series" and "second series" are shown in Table I. There have been only 2 "hospital" deaths among cases of infantile hydrocephalus treated by endoscopic coagulation in the last 6 years. (1 case of meningocele, and a case in which death occurred during subdural insufflation of air before operation, are not included.) In all of the patients operated upon, there has been an obvious decrease in intracranial pressure.

There is an interesting correlation between mortality and mentality. Of 10 patients with apparently normal mentality before operation there are 4 survivors after intervals of 5 to 7 years. In this group 1 death obviously resulted from operation, another was due to recurrence after a unilateral operation, and the remainder resulted from causes apparently unrelated to the condition.

In contrast of 20 patients known to have defective intelligence before operation, 17 are known to have died, in spite of the fact that the abnormal intracranial pressure was partially or wholly relieved by operation. The enlargement of the head existed at birth in 15 of these cases. This probably constituted a contraindication to operation.



Fig 1 Roentgenogram of skull of hydrocephalic infant, showing fenestration typical of 'idiopathic,' communicating hydrocephalus (Courtesy of Dr Cornelius Dyke)

Coagulation of the choroid plexuses has also been performed for the treatment of other conditions. In 6 cases, a large, sessile, ordinarily inoperable meningocele was brought to a manageable condition, but 5 of the infants died.<sup>1</sup> In 3 cases, the hydrocephalus resulted from a meningitis. All 3 died. Scarff (26) however, has had some successes in postmeningitic cases.

#### DANGERS OF THE OPERATION

The actual operative procedure carries surprisingly little risk. Collapse on the operating table has not occurred in the course of the second series. There has been only 1 death apparently due to hemorrhage or local damage to the brain in the recent series. Practically all of the other deaths in the new series have been due to digestive difficulties and respiratory infections, which are certainly often precipitated by the procedure. On the whole, the coagulation of the plexuses is about as well tolerated as is injection of air into the ventricles in comparable cases. Since the causes of death in individual cases have already been reported in previous communications (21, 22), and also by Scarff (26), a further discussion of them, therefore, appears to be superfluous.

<sup>1</sup>In 2 of the fatal cases death seemed to be unrelated to the operation. A further analysis of this group is in preparation.

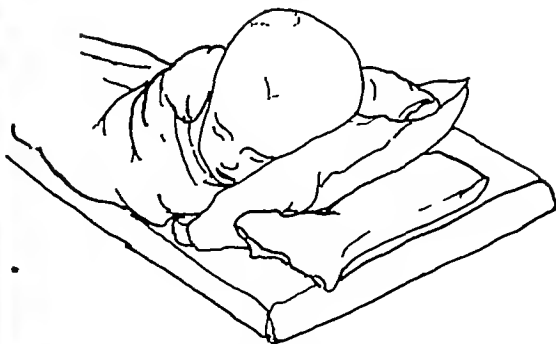


Fig 2 Arrangement of sandbags to secure the proper position of the patient on the operating table, with the operative field uppermost

#### FAVORABLE RESULTS

These can best be analyzed on the basis of a later follow-up report of the patients who were apparently normal at the time of operation. The last report on this group of cases was published in 1938 (23), and the case reports are numbered to correspond.

**CASE 1** Dorothy M. was apparently normal at birth except for a small meningocele in the lumbar region. She was operated upon, and the meningocele was repaired. The operation left her with a flaccidity of the right leg. When she was seen at the Children's Hospital, Boston, on May 14, 1934, at the age of 6 months, the head had reached a diameter of 20 inches (50.8 cm) and the fontanelles were bulging (Fig 3). The pressure recurred rapidly after ventricular puncture.

She was operated upon at the Children's Hospital on May 18, 1934. Coagulation of the right choroid plexus was carried out without incident, and the patient made a rapid recovery. The excessive intracranial pressure was at once relieved, judging by the fontanelles, and the size of the head returned to normal.

The patient has been seen from time to time since. She was sent to a home for crippled children, where a brace was fitted to the paralyzed leg.

The patient had a convulsion in December, 1939, and was transferred to the Monson State Hospital. Dr. L. J. Robinson of the Hospital Staff kindly replied to a letter of inquiry as follows: "Since her admission here, she has had but one seizure and that a petit mal. She has shown no evidence of increased intracranial pressure, although she has vomited on an average of twice a month without known cause. Her mental examination of December 6, 1939, revealed a chronological age of 6-1, mental age 5-2, intelligence quotient 84. As you know, she has a flaccid paralysis of the lower right extremity. She is now home on a visit."



Fig. 3. Case Dorothy M., before operation in June, 1934 (left) and in June 1941 (right).

Dorothy's mother writes as follows (June 14, 1941): "I am enclosing several snapshots taken during the past weeks (Fig. 3). You will readily note the improvement in her since last you saw her. She is healthy and strong and is very much over weight for child her age. Her shoulder and chest development are much in evidence due no doubt to

the use of her crutches. She is very bright, knowing what is taught her without effort, and has wonderful memory. When playing alone I sometimes hear her singing songs that she has learned one or two years ago. She is hearty eater and digests her food easily.

**CASE 2.** This case was reported in full in a previous communication. In brief J. F., infant of apparently normal intelligence began to develop signs of increased intracranial pressure at the age of 18 weeks. The enlargement of the head was progressive in spite of repeated ventricular punctures. At the time of operation (31 yr., 1934) the head measured 6 inches (15.2 cm.) in circumference at the age of 18 weeks. The right choroid plexus was destroyed. The intracranial pressure was temporarily relieved, and following operation the patient became bright and alert.

There was recurrence of increased pressure at time when I was out of town. A ventricular puncture was performed, and this led to intra-ventricular hemorrhage and death.

**CASE 3.** Daniel S. was born July 2, 1934, of healthy parents. He had a small meningocoele just in the cervical region, which grew rapidly so that plastic repair had to be carried out July 5 to prevent rupture. After the operation the head increased rapidly in size in spite of repeated lumbar punctures. The circumference had increased to 6 inches (15.2 cm.) on July 5 increased to 6 inches (15.2 cm.) on September 8. The fontanelle was tight, and there seemed to be no justification for waiting for further progress (Fig. 4).



Fig. 4. Case 3, Daniel S., before operation in September 1934 (left), and in December 1940 (right).



Fig 5 Case 4, Gail H, before operation, in September, 1935 (left), and in January, 1941 (right)

Coagulation of the right choroid plexus was carried out on September 10, 1934, at the Boston City Hospital. There was an immediate decrease in the size of the head, to 16 inches (40.6 cm).

The patient has been seen from time to time since. At the age of 3 years, he passed all of the Kuhlmann tests for his age, with the exception of those for coordination.

As of December 20, 1940, his mother writes: "Daniel is very well and is doing well in the first grade. I had a talk with his teacher who says he is very smart in his school work. Last week I took him to see Santa. I wish you could of been there to hear him talk up and tell just what he wanted for Christmas. For a child of his age, he sure can get some funny sayings out of him." Figure 4 shows the patient at this time.

CASE 4 Gail H, a girl referred by Dr. Charles McCann of Brockton, Massachusetts, was born by instrumental delivery after 56 hours of labor. A definite enlargement of the head was first noticed at the age of 6 weeks. When first seen at the Boston City Hospital on September 16, 1935 (age 2 months) the head measured  $17\frac{1}{2}$  inches (44.5 cm) in circumference, and the anterior fontanelle was bulging. A week later, the head measured  $18\frac{1}{4}$  inches (46.4 cm) and the child was distinctly more listless than before (Figure 5).

On examination, a drooping of both eyelids was observed. Aside from this, and the enlargement of the head, no abnormalities were made out. The baby appeared rather inactive. She responded to loud sounds but did not follow objects with the eyes, or reach for them.

Coagulation of the right choroid plexus was carried out on September 23, 1935. The pressure measured 320 millimeters of spinal fluid with the head elevated, the patient being under pentobarbital sodium anesthesia. A second operation had to be carried out on the other side, on October 22, 1935.

At 18 months, she passed all of the Kuhlmann tests for her age, and some of those for 2 years.

In January, 1941, her mother reports as follows: "Gail is the youngest of a class of 15, but she holds her own with the best of them. Her arithmetic and spelling are exceptionally good. She was a little slow



Fig 6 Case 5, Peter R, in May, 1939, 2 years after operation and shortly before death



Fig. 7. Case 4, James F. before operation in 1937 (left) and about January 1941

getting started in reading. The teacher is very pleased with her progress and thinks she will make the second grade in public school next September. A photograph taken about this time is shown in Figure 5.

**CASE 5.** Peter R. was born June 5, 1936, with large meningocele of the lumbar region, which was operated upon in another city when he was few days old. Following the operation, there was some weakness of the sphincters and of the legs, which slowly improved. The head became definitely enlarged at the age of 3 weeks. At the age of 10 months, it became definite and progressive.

He was brought to the Boston City Hospital on April 7, 1937. At that time the head measured 30 inches (50.8 cm.) in circumference.

On April 8, 1937 the patient was operated upon. The pressure as measured at 300 millimeters of spinal fluid, calculated from the tip of the needle with the head elevated on a pillow. A second operation was carried out May 3 on the other side. The head decreased slightly in size and the patient appeared distinctly more bright. Details of the examination and photographs are given in the previous communication (3).

The baby returned to his home in the tropics, and did well at first. On May 6, 1938 his head measured 35 inches (54.6 cm.) and the strength of his legs improved. A photograph taken May 3, 1939, is shown in Figure 6. A spot of this patient's progress, he had a convulsion and died on May 6, 1939.

**CASE 6.** James E. was born on July 7, 1937 at 7½ months. He was otherwise well until about the age of 3 months, when the family physician Dr. Thomas Shea of Holyoke, Massachusetts, noticed that the head was enlarging. The baby was seen by Dr. Jerome Whitney of Springfield, who recommended his admission to the Boston City Hospital for operation. Measurements of the head were as fol-

lows: August 7, 46 cm. (18½ inches); September 4, 47 cm. (18¾ inches); October 6, 49 cm. (19½ inches). The proportionate enlargement of the head was obvious (Fig. 7) the scalp veins were dilated and the fontanelles were bulging. There were no obvious neurologic abnormalities, and the infant was able to carry out the normal performances for his age.

He was operated upon for the first time on October 3, 1937 under nembutal anesthesia. The pressure was measured at 300 millimeters of spinal fluid, from the tip of the needle with the head raised. The cortex was about centimeter thick. The right choroid plexus was thoroughly cauterized. There were no postoperative complications but within a week it was obvious that the pressure had not been completely relieved. Accordingly the left choroid plexus was cauterized on October 5, 1937. At this time the pressure was measured at 200 millimeters of spinal fluid.

The patient was very little disturbed by the second operation. His head decreased in size and he appeared distinctly more alert. He was discharged and did well for 6 months. At the end of that time the parents observed that the head was growing larger again.

Accordingly the site of operation on the right was re-explored on December 7, 1937. Under the dura in a pool of dark yellow fluid, at a pressure of about 35 millimeters of mercury. This fluid contained 300 milligrams of protein, and about 30 cubic centimeters of fluid drained away. The wound was closed tightly. During the following 4 weeks, the subdural space was punctured and drained every other day. Decreasing amounts of fluid were drained, and finally toward the end of December no more accumulated.

The patient made good progress on the table during the next 3 years. He grew normally although the head was evidently slightly larger than the rest

age. He appeared bright and alert, but was slow in learning to walk.

In November, 1930, he became restless and slept poorly. The head seemed to be growing again—measuring 23 inches (58.5 cm) on December 24, 1930. At the request of Dr. Edward Bagg of Holyoke, he was admitted to the Neurological Institute of New York for study, on January 8, 1940. At this time, the circumference of the head was 60 cm (23.5 inches). There was a slight turgescence of the veins of the scalp. The patient showed a static ataxia but neurologic examinations otherwise not remarkable.

A complete psychometric examination was performed by Miss Marion Corwin. Her summary is as follows: "Tests on this child are unsatisfactory because of his physical handicaps. He shows very poor motor coordination. Apparently a visual defect interferes with his response to pictorial material, but an occasional response suggests good grasp of that which he does see. His use of language might suggest an acceleration in development, but one rather imagines that because the child's possible activities are so limited, he has found conversation with adults especially stimulating and thus has achieved a greater development in this field than he would have achieved if he had more outlets. A single score has little value in a child whose development is so uneven, but one has the impression that he is correctly placed in the average group."

In addition, a ventriculogram was performed, which showed a moderate enlargement of the ventricles, a suggestion of block at the fourth ventricle (Fig. 8). The pressure, however, appeared to be within normal limits. The patient was discharged without treatment.

Since that time, he has done well. In January 1941 (age of patient, 3½ years), his mother reported by letter as follows: "His step appears very wobbly and uncertain and the slightest thing will throw him and he loses his balance temporarily for no apparent reason, grabs and holds and refuses to go on without assistance. Some days he does much better than others. His head measures 58½ cm, although his hair at present is very thick, height 40 inches, weight 42 lbs. In his wagon, he will put his groceries, pull them around, ask me, 'What I want today?' I'll tell him and he'll pick out just what I asked for and keep on going and if a neighbor passes by, he'll ask them also (this is on the porch), he knows everyone by name and can he ask questions. He is very good all day and while I'm busy working, he is in his play pen amusing himself wholeheartedly, providing I am not in the kitchen, if I am he wants to help me do whatever I'm doing, mashing potatoes, drying the dishes, straining orange juice, etc."

A photograph taken about this time is shown in Figure 7.

The statistics and case reports speak for themselves. It now seems well established that coagulation of the choroid plexus regularly reduces the intracranial pressure, and



Fig. 8 Encephalogram of James E., made in January, 1940

that the relief is sufficient in most cases of infantile hydrocephalus to prevent death from pressure. Further, it seems clear that those patients who show a reasonably normal mentality at the time of operation usually make a good operative recovery, and have an excellent chance of growing up normally. To explain the results as due to a coincidental spontaneous recovery is to overlook three important facts: first, that the intracranial pressure was progressive before operation, obviously endangering the infant's brain, in all the cases here reported, second, that the intracranial pressure was decreased by the operation not only in these, but in all patients operated upon by the endoscopic technique, third, that the proportion of recovery from hydrocephalus was higher, both in this series and in that of Scarff (26), than has ever been reported in untreated cases.

#### SUMMARY

1 The present technique of endoscopic coagulation of the choroid plexuses in the treatment of infantile hydrocephalus is described.

2 A history of the operation as carried out by others, and of its theoretical background is presented.

3 The results of the operation are analyzed statistically and a group of favorable cases is presented

4 It appears that only infants with approximately normal mentality are likely to survive the operation.

5 In view of the fact that the operative mortality is now low and that patients who can be shown to have normal mentality usually do well after operation the conclusion seems justified that coagulation of the choroid plexuses should be tried in all cases of infantile hydrocephalus in which a reasonably normal intelligence can be demonstrated unless other complications exist.

#### REFERENCES

- 1 BACON P. C. Hydrocephalus. I. Practice of Pediatrics (Brennenman) Vol. 4, Chap. 3, pp. 3-27 Hagerstown, Md. W. F. Prior Co. Inc. 1931
- 2 BERNARD, CHARLOTTE, and HERRIS, HILDEGARD. Testing Children. Development from Birth to School Age. New York: Farrar & Rinehart, Inc., 1933
- 3 CATHART, A. C. Die Medizinische Klinik. IV. Mollenat edition. P. 50. Edinburgh: MacLachlan & Stewart, 1871
- 4 DAVIS W. Article, Hydrocephalus. In Lewis, D. Practice of Surgery Vol. 4, Chap. 4, Sec. 5, pp. 3-233 Hagerstown, Md. W. F. Prior Co. Inc. 1932
- 5 IDEM. Ann Surg. 1934, 104: 104-107
- 6 IDEM. Ann Surg. 1934, 99: 500
- 7 IDEM. Bull. Johns Hopkins Hosp. 1932, 31: 74
- 8 DODD W. and BLACK, N. K. D. J. Am. M. A. 1933, 6: 6
- 9 DODD L. Arch. Surg. 1930, 8: 717-722
- 10 DODD L. Neurological Surgery Philadelphia: Lea Febiger 1936
- 11 FERRIS, ALBERT. Surgery 1934, 4: 245-246
- 12 FLETCHER, T. and GALT, F. C. J. Am. M. A. 1934, 46: 1461
- 13 FLEMING, J. A. Two tests for young children. In University of Iowa. Studies in Child Welfare, Vol. 4. Iowa City: University of Iowa, 1931
- 14 FLEMMING, F. and DODD, W. H. Arch. Surg. 1934, 80: 190
- 15 KILM, J. A. Handbook of Mental Tests. For their Revision and Extension of the Bureau Scale. Baltimore, Md. Warwick & York, Inc. 1931
- 16 MADDY, W. Ann. J. Dis. Child. 1934, 29: 474-475
- 17 MINNER, W. J. Boston M. & S. J. 1933, 38: 17-18
- 18 MINNER, D. P. Ann. J. Obst. 1937, 34: 40-45
- 19 PEARCE, W. Surg. Gyna. Obst. 1935, 60: 77-78
- 20 IDEM. Ann. J. Dis. Child. 1935, 30: 13
- 21 PETERS, T. J. N. England J. M. 1934, 70: 57-58
- 22 IDEM. Arch. Pediat. N. Y. 1935, 51: 64-65
- 23 IDEM. Ann. J. Dis. Child. 1937, 35: 600-605
- 24 RUSSELL, DONOVAN S. and CHAMBERLAIN, DONALD. London 1933, 58: 207-211
- 25 SCARRY, J. E. Arch. Neu. Psychiat. 1934, 35: 829-834
- 26 IDEM. Ann. J. Dis. Child. 1935, 33: 297-304
- 27 SCHULTZ, T. Die Krankheiten der Mund- und Rachenhöhle. I. Vorklinik. II. Hygiene. III. Therapie der Krankheiten. Vol. 9. Part 5. G. J. F. Hoesler, 1930
- 28 SCHULTZ, T. Strahlentherapie 1934, 27: 70

# NON TUBERCULOUS EMPYEMA THORACIS IN CHILDREN

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**I**N a previous communication (1) the value of fluoroscopic examination as a method for determining the proper time for rib resection in empyema thoracis was discussed. This method has become increasingly valuable since the advent of the sulfonamide drugs in the treatment of pneumonia. It is valuable not only as a guide to treatment but also as a means of accurate diagnosis.

## INCIDENCE OF THE DISEASE

From January, 1936 to June, 1942 a total of 184 patients of empyema thoracis has been admitted to the Riley Hospital. In 1936 there were 5 cases, in 1937 33, in 1938 28, in 1939 22, in 1940 17, in 1941 23, and for the first 6 months of 1942 there were 17 cases. Sulfonamide drugs were not used in any cases in 1936 and 1937. Since 1938 their use has greatly increased until in 1941 and 1942 practically all patients received the *e* drugs. Although some observers (2) believe that the incidence of empyema has increased with the use of sulfonamides, our study seems to indicate that this complication varies in number and severity from year to year and as yet has been uninfluenced by the *e* drugs.

Our survey does show as pointed out by others (2, 3) that empyema occurs in a masked and often bizarre form more frequently since the use of the sulfonamides. This is evidenced by the fact that in 1936 and 1937 65 per cent were general and 7 per cent were interlobar or encapsulated, and 1 per cent were bilateral. In 1941 and 1942 75 per cent were general, 25 per cent were of the latter type, and 1 per cent were bilateral (Fig. 6).

## TYPES OF ORGANISMS

The type of organism causing empyema varies from year to year. In 1936 the following varieties of bacteria were responsible—streptococcus, 5; hemolytic streptococcus, 3;

pneumococcus, 38; gram positive bacilli and streptococcus, 1; no growth, 1. In 1937 there were *Staphylococcus aureus*, 2; nonhemolytic streptococcus, 2; *Staphylococcus epidermidis*, 1; *Staphylococcus aureus*, 2; no growth, 1; and pneumococcus, 20—divided into the following types—type I, 15; type V, 2; type VIII, 1; type I and III, 1; not given, 1. In 1938 there were *Staphylococcus aureus*, 2; nonhemolytic streptococcus, 5; pneumococcus, 12 of the following types—type I, 8; type III, 1; type V, 3; sporadic to transform bacilli and nonhemolytic streptococcus, 1.

## TREATMENT

Once empyema has occurred the sulfonamides do not aid in the cure of the disease. The pus must be evacuated by aspiration, closed or open drainage. Rib resection and open drainage were done in 80 per cent in 1936, 50 per cent in 1937, 80 per cent in 1938, 91 per cent in 1939, 90 per cent in 1940, 96 per cent in 1941, 100 per cent in 1942. Repeated aspirations were done in 14 cases, closed drainage was done in 3 cases. Two of these were later operated upon by rib resection. Spontaneous resolution was not observed before or since the use of sulfonamides. However, it should be said that in the streptococcus varieties localization is hastened by the use of the drugs.

Anyone who has treated children with empyema has been impressed with the necessity of early open drainage in preventing complications such as suppurative pericarditis, multiple pocket formation, chronic empyema and septicopyemia. They must also be aware of the danger of open drainage before localization has occurred.<sup>1</sup> Formerly the proper time for such drainage was based upon the consistency of the pus obtained by aspiration. However, we have observed that pus may be thick very early in the disease when sulfonamides have

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<sup>2</sup>Since submitting this paper for publication we have observed a case of putrid empyema following lung abscess. Fixation of the diaphragm and mediastinum was present on admission to the hospital. Since many of the causative organisms in such patients are anaerobes, immediate open operation is imperative.





Fig. 2. Diagram indicating normal excursions of the diaphragm and mediastinum as observed by fluoroscopic examination. *D*, Diaphragm; *M*, mediastinum. 1. Diaphragm descends and mediastinal shadow is narrower on inspiration. 2. Diaphragm ascends and mediastinal shadow is wider on expiration.

been used. Lanman and Heyl have reported similar observations. This change in consistency may precede localization. Furthermore we have found in children not treated by such drugs that localization may occur before the pus becomes thick. (1) Burford and Blades point out that the transition from effusion to frank pus is prolonged in cases in which sulfonamide therapy has been employed. Our experience seems to substantiate the observation that the illness is prolonged although here again great seasonal variations are noted. In 1936 the average hospital stay for patients treated by rib resection was 34 days. The average stay before operation was 11 days and after operation 53 days. In 1941 the average hospital stay for patients treated by rib resection was 49 days. The average stay before operation was 11 days and after operation 38 days. In 1942 the average hospital stay was 40 days before operation 14 days, and after operation 26 days. The clinical and laboratory symptoms and signs such as the temperature, the appetite and leucocyte counts cannot now be relied on. When the temperature was of the septic type, the appetite poor and there was a high leucocytosis one felt sure that pus was under pressure and should be drained. However the fever curve is no guide when the sulfonamides are given and they produce anorexia in most children. Also the leucocyte counts may not be reliable as guides for surgical intervention when these drugs are used.

#### FLUOROSCOPIC OBSERVATION

In his splendid review of the literature on nontuberculous empyemas, Ehler thought that our method would provide valuable information concerning the proper time to "drainage" but that "the interpretation of its findings requires considerable experience and familiarity with intrathoracic dynamics." During the past 6 years we have developed some practical maneuvers in the fluoroscopic examination of empyema patients, which has greatly simplified this method.

The fluoroscope is important to determine (1) whether or not localization has occurred and (2) the position of the encapsulated or interlobar varieties of empyemas. The method is based upon the fact that with localization comes fixation of the walls of the empyema cavity. In children as we have stated empyemas are usually massive so that fixation of the movable diaphragm and mediastinum are accurate guides. The mediastinum does not change as much in adults. However, even in localized cavities the phenomenon of fixation of the surrounding lung can be demonstrated.

In the normal child the diaphragm descends on inspiration and the mediastinal shadow becomes narrower. On expiration the reverse is true (Fig. 2).

In the child with empyema a thoracentesis is done to determine the type of organism, partially to empty the cavity of pus, and also to inject air. First the child is observed in the upright position. The fluid level is easily seen and before localization moves with respiration (Fig. 3). It descends with the diaphragm on inspiration and ascends on expiration. After localization two phenomena have been observed: (a) no movement—this is seen in bilateral and sometimes unilateral empyema; (b) paradoxical movement—this is seen in unilateral empyema due to an exaggerated movement of the opposite leaf of the diaphragm. We believe that the large excursion of the unaffected diaphragm increases intra-abdominal pressure on inspiration and forces the fixed side upward—the converse may be true during expiration (Fig. 3).

It would be impossible to observe the movement of the diaphragm with the patient in the flat or upright position because pus obscures

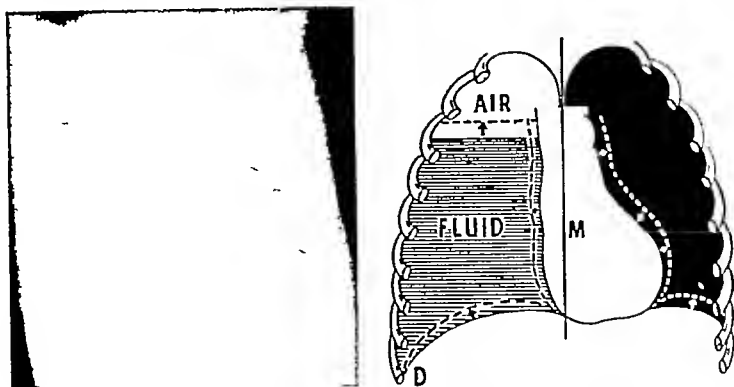


Fig 2 Empyema of right pleural cavity. The child is in the upright position. Fixation has not occurred. On the left is an x-ray photograph, on the right a diagram illustrating fluoroscopic observations. Both leaves of the diaphragm and both sides of the mediastinum move with respiration. As the diaphragm descends on inspiration the fluid level moves down and on expiration it moves upward.

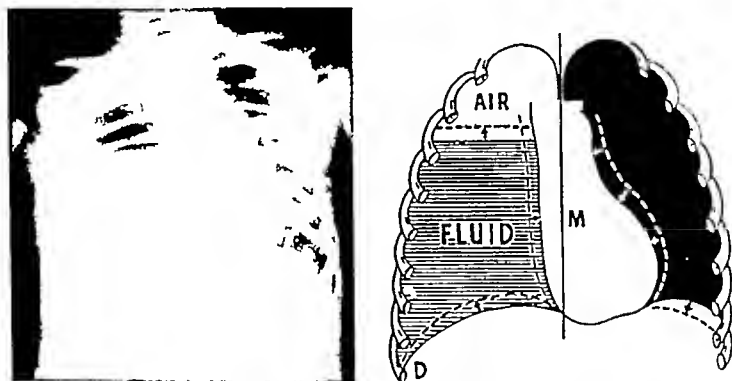


Fig 3 Patient in upright position. Empyema thoracis (right) after fixation. Paradoxical movement with deep inspiration: the left diaphragm descends and the left mediastinal shadow moves mesially. The right diaphragm ascends and the fluid level moves upward.

the contour of the diaphragm and on the right side the liver also adds its dense shadow, making such observation difficult (Fig 2). However, with the patient tilted in the head-down (Trendelenburg) position the diaphragm can be seen easily if a sufficient amount of air is present in the empyema cavity (Fig 4). Small amounts of air are seen in the costophrenic angle only and are of no aid, 20 to 30 cubic centimeters of pus or more is aspirated and an equal amount of air is injected. Fixation of the diaphragm implies localization.

A third maneuver enables us to observe the mediastinum. The patient is turned on the

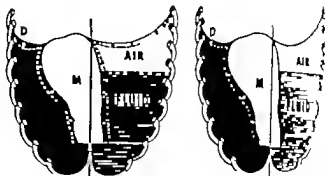
affected side and is observed in the anteroposterior (lateral decubitus) plane. The pus gravitates away from the mediastinum permitting observation of its movements. If this is fixed the cavity is completely localized and open drainage may be safely done (Fig 5).

#### MORTALITY

In our previous study we reported 123 cases of nontuberculous empyema caused by the pneumococcus, streptococcus, and staphylococcus in which patients were treated with fluoroscopic observation, and of which 100 had rib resections. The mortality in this group was



Fig. 4. The patient is in the Trendelenburg position. On the left is roentgenogram. On the right are diagrams illustrating fluoroscopic observation of the diaphragm. The center illustration depicts movement of the diaphragm



cephalad (arrow) during expiration, air space dense. It is the movement of the diaphragm that is elevated. Illustration on right shows fixation of diaphragm. X-ray of admission to diaphragm in the roentgenogram.

4.9 per cent. We also reported 27 cases in which patients were treated by early rib resection which was possibly due to the aid of fluoroscopic examination. There was no mortality or complication in this group and the hospital stay was much shorter. No irrigations were employed. The fluoroscope was also used to determine the proper time for removing the tube. When no fluid could be seen the tube was removed. This was possible in 8 to 10 days in pneumococcal types.

Mortality rates since 1936 were as follows:

	Cases	Deaths	Per cent
936	45	4	8.8
937	55	3	5.5
938	8	4	4
939			4.6
940			8.1
941	5		4
942	7		
Totals	54	4	7.6

An analysis of these deaths shows that of the 167 cases in which patients were treated by rib resection there were 5 deaths, a mortality rate of 2.9 per cent. The deaths in this group were as follows: (1) a boy aged 5 years with perforated appendicitis spreading peritonitis subphrenic abscess and *Bacillus coli* empyema. (2) streptococcal empyema in a 7 month old girl with brain abscess. (3) pneumococcal empyema in a boy 2 years old with cerebral embolus. (4) pneumococcal empyema in a girl aged 2 with pneumonia in opposite lung. (5) a boy aged 2 years with rheumatic heart disease and type VIII pneumococcus empyema.

There were 9 deaths in patients treated by aspiration or closed drainage. These were as follows: (1) an 8 year old girl with pneumococcus empyema *in extremis* who died 2 hours after admission to the hospital. (2) a 1 year old boy with hemolytic streptococcus empyema following scarlet fever and bronchopneumonia who also had interstitial nephritis. (3) a 13 year old boy with chronic suppurative otitis media, mastoiditis, and septicemia who had received prontosil. (4) a 6 year old boy with perforated appendicitis, peritonitis, liver abscess, pneumothorax, spontaneous subcutaneous emphysema. (5) a 1½ year old girl who entered the hospital with a temperature of 107 degrees and a leucocyte count of 37,000 (type VI pneumococcus was isolated from sputum) died 2 hours after admission. (6) an 11 year old boy with type V pneumococcus empyema who died 48 hours after admission. (7) a 2½ year old girl with type V pneumococcus who had received sulfapyridine and died 34 hours after admission. (8) a 3 day old boy with *Staphylococcus aureus* empyema whose death was due to staphylococcus septicemia and who had received sulfathiazole. (9) an 11 month old girl with type V pneumonia and empyema who received sulfathiazole and whose death occurred 3 days after admission. Most of the deaths—7 per cent—occurred before the advent of the sulfonamide drugs. However in our previous study we reported 27 consecutive cases in 1935 without a death or complication. This is indicative again of the



Fig 5 Empyema thoracis (right) observed with patient in lateral decubitus position. On the left is a roentgenogram showing the fluid level after aspiration and injection of air. On the right is an illustration depicting the movement of the diaphragm and mediastinum. With expiration the diaphragm moves upward and the mediastinal shadow widens (see arrows). The air space is narrowed. It is the movement of the mediastinal shadow that is observed. After fixation there is no mediastinal movement on the affected side.



Fig 6 Localized types of empyema. a Small encapsulated cavity, b interlobar empyema in fissure between upper, middle and lower lobes at the level of the fifth rib.

great yearly variation in the severity and frequency of the disease.

It should be noted that the children treated by aspirations or closed drainage were either in too critical condition for open operation or, if observed by the fluoroscope, it was found that localization had not occurred and therefore the open operation could not be done.

#### COMPLICATIONS

The number of complications varies from year to year. However, there does seem to be a

decrease since the sulfonamides have been used. In 1936 in addition to the 4 deaths reported, the following complications were observed: draining sinus, 1; pneumonia on opposite side, 1; chronic empyema with toxic arthritis, 1; bronchial fistula, 2; and 2 children were admitted because of chronic empyema—15.5 per cent of the patients treated. In 1941 and 1942 in addition to the 1 death reported, there were 1 subcutaneous abscess, 1 glomerulonephritis, and 1 bronchopleural fistula—7 per cent of the patients treated.

## SUMMARY

1 Rib resection with open drainage is the method of choice in treating empyema thoracis in children

2 Since the advent of the sulfonamide drugs the use of the fluoroscope is necessary to determine the proper time for this procedure. This is true because other criteria such as the character of the pus, leucocyte counts and temperature range are not reliable guides when the sulfonamides are employed

3 Methods of fluoroscopic observation are described

4 A study of 184 cases of empyema before and since the use of the sulfonamides reveals the following observations (a) The incidence

of the disease varies from year to year (b) is apparently uninfluenced by their use (c) there is a greater incidence of localized type (d) empyema (e) streptococic and staphylococic varieties are not as serious as formerly (f) the stay in the hospital is prolonged (g) the mortality is much less (h) complications are less frequent

## REFERENCES

1. BEAN, J. K. *J. Indiana M. Ass.* 34 (4, 1931) 401  
*Am. M. Ass.* 96, 97, 98
2. HARRISON, THOMAS H. and B. L. LEE, JR. *J. A. M. A.* 94, 3, 95
3. ELLER, ALICE A. *Surg. Gyn. Obst.* 44 (1927) 641-7
4. L. W. & THOMAS H. and HARRISON, JR. *J. A. M. A.* 93, 100

# INJURIES OF THE PARIETES AND EXTREMITIES

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## The Care of Wounds under Emergency Conditions

IN the foregoing discussion of wound treatment it is assumed that the patient comes to the surgeon promptly after injury and that there are adequate facilities, assistance, and time to permit him to carry out the surgical procedure indicated. When one is suddenly confronted with a large number of injured patients, as after a fire, explosion, tornado, and air raid or under conditions of war, one must adapt the treatment to the conditions at hand. Organization and foresight can help immeasurably though no amount of planning and preparation is effective unless cool heads are available when the critical moment arrives.

Under conditions of stress and with inadequate facilities for carrying out surgical treatment one can accomplish the greatest good for the greatest number by giving skillful first aid care and sending patients as promptly as possible to hospitals where adequate surgical care can be given.

What constitutes the simplest form of skillful first aid treatment? The removal of any free foreign bodies, implantation of a sulfonamide in the wound so that its bacteriostatic action may arrest bacterial activity, the application of a large sterile dressing, bandaged with moderate pressure, and of a splint to immobilize the injured extremity. For the majority of patients such primary treatment is adequate. For the complications which demand immediate attention, namely shock and hemorrhage, special provision must be made.

If well planned, emergency treatment can be carried out rapidly and efficiently for a large number of patients and with a minimum number of highly trained personnel. In other words nurses, hospital orderlies, and the per-

sonnel of medical regiments under the direction of only a few surgeons can render invaluable aid if the principles stressed above are kept in mind, namely, not to add infection to the open wound, not to add further trauma.

It is not difficult, for example, to visualize an "assembly line" which consists of very simple equipment: two or three rows of wooden supports upon which stretchers can be rested, and opposite them tables with sterilizing units, instruments, sterile dressings and material for splints (Fig. 26). At the entrance to the tent or hut is a supply of masks, and as the stretcher is put down before the examining surgeon, stretcher bearers and patient are masked. Needless to repeat, all personnel within the tent or hut are masked.

The surgeon, one of the most experienced men of the group, must decide quickly whether the patient should be taken immediately to the "shock tent" *A*, whether he should be taken to the surgeon at *B* because his blood soaked dressing indicates that active bleeding is going on, or whether he can be entrusted for the application of the dressing to trained nurses and orderlies at *C*. If after the patient's dressing is applied he requires more than a simple immobilizing splint he can be taken to *D* where the splint team is provided with equipment for immobilizing fractures of long bones and for complicated cases.

Such a unit could function with only a few well trained surgeons: one as diagnostician to decide what should be done immediately, one to care for patients with bleeding wounds, one to supervise the whole, to direct the treatment of shock and supervise the application of dressings and of splints. An anesthetist to aid the operating surgeon with nitrous oxide or an intravenous anesthetic, and a dental surgeon skilled in the use of plaster to direct the splint team could give invaluable assistance.

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Part I of this article appeared in the January 1943 issue, pp 1-22.

Obviously such a simple scheme could be expanded indefinitely in proportion to the personnel and equipment available. Experienced surgeons would agree however that under emergency conditions several units of relatively small size and physically separated can render more efficient service than a single large unit which may easily be handicapped by lack of adequate facilities for entry and exit and for transporting patients.

In the first World War for example it was found advantageous to arrange casualty clearing stations in groups of two or three. In times of stress one station would admit 100 or 200 patients and then the stream of wounded be diverted to the next station so that a bottle neck would not develop near the head of the line due to difficulties in caring for the patients first admitted.

Not the least important element in the success of a plan for caring for a large number of patients in a short period of time is the choice of a site for the first aid station. It should be placed so that ambulances and trucks can be unloaded and leave without interfering with incoming vehicles and permit evacuation of treated patients without interfering with the transport of incoming patients. The most efficient use of transport would result if ambulances freed of their load of incoming patients could pass on to the exit of the station and take on patients ready for evacuation to hospitals where adequate surgical care could be given.

#### CHEMOTHERAPY IN THE TREATMENT OF WOUNDS

Many investigators have emphasized the fact that bacterial contamination is a common occurrence in open wounds whether accidental or the result of surgical incision. Ives and Hirschfield for example reported that in 30 clean surgical cases bacteria were recovered from all the wounds. In a recent study Pulaski, Meloney and Spaeth found bacteria present in every one of 200 fresh untreated traumatic wounds. In neither report was it stated what percentage of the organisms found were pathogenic. In Ives and Hirschfield's series infection developed in only one case. No statement is made in Pulaski, Meloney

and Spaeth's paper as to the result of treatment except that "no cases of gas gangrene and no cases of tetanus developed in the 15 from which these organisms were grown (4 cases, 23 per cent of the total) treatment being instituted to prevent their activity."

The general recognition of the fact that bacteria are constant contaminants of open wounds has been the dominating factor in the constant search for means of destroying the bacteria and this effort, often directed by individuals without surgical training has infrequently ignored certain fundamental facts, namely that not all bacteria present in open wounds are pathogenic that even as ago man was forced to develop an effective immunity to pathogenic bacteria and that this natural defensive mechanism is not effective when body tissues are injured, when no blood clots are present in the wound and when the affected part is kept at rest.

Furthermore as L. Ives and Burbank have pointed out in their excellent review of local sulfonamide therapy successful chemotherapy depends upon the specific effect of a drug upon a specific infectious agent, as exemplified in the treatment of syphilis and malaria.

"The topical application of sulfonamide drugs is contrary to this fundamental concept of chemotherapy in all respects. First, there is established locally concentration of drug known to be not systemically. Secondly it is proposed to hasten the action of the drugs to include as effect on relatively insensitive bacteria by increasing the concentration of the chemical group. The proposal to use sulfonamides as prophylactic agents against polymicrobial wound infections merits rather departure from conventional thinking. Future data demonstrate that systemically toxic concentrations of sulfonamides are at least locally tolerated and that wider antibacterial action is achieved by these higher concentrations. In emphasizing the importance of this work the emphasis should be upon the broadened concept of chemotherapy rather than upon sulfonamides."

"There is still a lack of critical evidence regard to the effect of locally implanted sulfonamides upon wound healing. Apparently the cell can recover from the toxic effects of sulfonamide if transferred to an environment completely free of the drugs but there is no information as to the rate of recovery of poisoned cell upon transfer to a medium containing a lower concentration of drug. The variable factors of solubility and local persistence of the drugs and the advisability of parenteral therapy





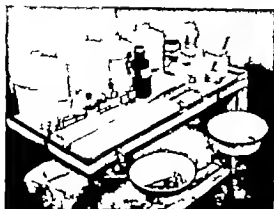


Fig. 7 Left, A dressing cart is of invaluable service in helping to apply dressings quickly and easily and to maintain an aseptic technique. The porcelain jars contain (from left to right) sterile towels, large dressings, 4 by 4 inches, smaller dressings, 3 by 3 inches, sterile applicators, medicine glasses and tongue blades. Safety pins, benzene, 95 per cent alcohol, soap solution, colloidion, Dakin's solution in dark brown bottle and boric solution in flask stand in front of the jars. Petroleum grease is kept in the smaller covered porcelain tray and sterile instruments in the larger. Sterile petroleum and zinc oxide ointment are kept in small covered porcelain containers. Cast cutting knife, bandage scissors and dressing forceps in wooden jar are

easily accessible. Bins on arms, back being suitably under the top section, contain for quick removal. On the lower shelf are large sterile pads wrapped in sterilized paper, sterile basins, gloves, sterile absorbing syringes, water, renalin, bandages, and large bins for solid dressings. A paper bag strapped to the end of the cart carries a newspaper on which to lay soiled dressings as they are removed from the wound.

Fig. 8 Before dressing is applied, sterile towel is on the bedside table and on it instruments and soiled dressings. With a little practice one can change dressings quickly and still have it sterile, except for the surface layer and so fingers free from soiled wounds.

2. In what proportion of open wounds are such bacteria present?

3. What is their source?

4. Can these bacteria be eliminated in greatest part by simple mechanical cleansing that does not injure living tissue?

5. If simple wound cleansing is effective within a hours after injury how long after wound is it still effective?

6. Do chemical agents—the sulfonamides in particular—prevent the development of infection in a wound contaminated with pathogenic bacteria?

7. How can they be used to best advantage?

Many serious efforts are being made to find the answer to these questions, and it is not too much to hope that a definite, logical and more effective method of preventing infection of open wounds than has been available in the past will be evolved in the near future.

#### INFECTED WOUNDS

The care of infected wounds is so well described in modern textbooks of surgery that it is needless to discuss it again in detail. A brief summary of the surgical principles in

involved, however, may add to the completeness of a discussion of the treatment of wounds.

With infection present in an open wound the first problem is one of diagnosis. Before logical and effective treatment can be initiated the surgeon must answer three questions.

1. Is the infection a diffuse spreading infection or is it localized?

2. If it is localized, what is the site of localization?

3. What is the causative organism or organisms.

It is a well recognized surgical principle that in the presence of an acute spreading infection except in some types of infection due to anaerobic bacteria, active surgical treatment is contraindicated and the patient will achieve the best results by abstaining from operation and by doing everything in his power to increase the patient's resistance. To combat the infection by specific chemotherapeutic agents, if such are available, is to employ local treatment which will help to limit and localize the infection. Absolute maintenance of fluid intake, of nutrition and elimination are cardinal and all recovery

obligations. Specific chemotherapy of the causative organism is known, blood transfusion from immunized donors (Laxons) and in certain cases the use of heparin can be of very great help. Sulfanilamide and sulfadiazine have proved to be of lifesaving value in cases of acute spreading streptococcus infection, the most common and most dreaded form of acute spreading infection. Sulfathiazole, heralded as of particular value in staphylococcus infection has not proved as effective as had been anticipated. The control of staphylococcus infection is still a baffling problem. Recent work with penicillin has given promising results and the first report of its clinical use on a large scale appeared recently in a preliminary report by Laxon and Churchill of the treatment of a large group of burned patients at the Massachusetts General Hospital. Locally, the application of large warm wet sterile dressings that help to maintain the circulation at a maximum and elevation of the affected part to aid in the return circulation and delay the onset of passive congestion are of definite value in helping to bring about localization of the infection and in relieving the pain of acute inflammation.

The symptoms of an acute spreading infection are familiar to every third year medical student: high fever, rapid pulse, prostration, diffuse inflammatory reaction of skin and soft tissues, increasing in extent and intensity as the hours go by, and red streaks extending proximward from the site of infection—warning signals of a virulent infection spreading along the lymphatic vessels.

Confronted with such a picture it is obvious that the surgeon is dealing with a diffuse invasive process which cannot be helped by local incision, but which may be greatly aggravated by any surgical interference with nature's effort to combat and localize the infection. Since it is often impossible quickly to identify the cause of the infection one must resort to the empirical use of sulfonamides because of their demonstrated value in arresting rapidly spreading infection, but remembering that the available drugs may not be specific for the infection present, that some organisms are sulfonamide resistant, and that although the causative organisms may be rendered

bacteriostatic by the drug given the mechanism that destroys bacteria in the blood stream and body tissues may not function normally and the infection may continue and progress. The importance of giving sulfonamides in sufficient amounts to secure as promptly as possible a blood concentration of 7 to 10 milligrams per cent has been stressed repeatedly by Long, Lockwood, and many others. The necessity for maintaining adequate fluid intake and elimination and for watching the patient carefully for signs of toxemia, retention and renal involvement has been repeatedly emphasized.

In the presence of localized infection the surgical principle of *securing adequate drainage with minimum injury of essential structures* is the first consideration. This necessitates accurate diagnosis as to the site of infection. In some cases the diagnosis may be obvious, in others recognition of the exact location of an accumulation of pus requires thoughtful consideration and interpretation of the symptoms the patient presents. Many a hand, for example, has been irreparably injured because of the failure to make a correct diagnosis as to the location of pus formation, and secondly, by failure to consider how the infected area might be drained with minimum injury to soft tissues, nerves, blood vessels, and tendons.

After an infected area has been drained the wound must receive cleanly surgical care until healing is complete (Figs 27, 28). One of the commonest errors in surgical practice, both in hospital and office is the addition of further infection to that already present. Just as in the immediate care of open wounds unmasked faces, unclean hands, instruments incompletely sterilized carry a constant threat for the patient with an open wound. Anyone who has seen the telltale bluish-green color of pyocyanus infection appear on the dressings over a wound, and watched the appearance of the identical color on the dressings of one patient after another throughout the ward cannot doubt that the streptococcus, staphylococcus, and other types of virulent organisms can be carried from one patient to another in the identical fashion in which the *Bacillus pyocyanus* is so often inoculated in the wounds of successive patients.

## UNUSUAL TYPES OF INFECTION

A special word should be added concerning unusual types of infection, because they demand unusual treatment.

Gas gangrene is a spreading infection, often rapidly spreading, which in contrast to rapidly spreading pyogenic infections, requires active surgical treatment. A foul smelling discharge which in the early stages may consist only of hemolyzed blood, from a wound received on the street, on a dirty road, or as the result of a penetrating injury and particularly if the injury has been of a crushing nature and has involved muscle tissue should always suggest the possibility of infection with a virulent anaerobic organism of the group typified by the *Clostridium welchii*. If in addition to the characteristic wound discharge and history of injury the edges of the wound are blackened and the skin about it mottled with a greenish yellow discoloration similar to that resulting from breaking down of blood cells in the subcutaneous tissues, one can be fairly certain that microscopic examination and cultures of the wound discharge will show the characteristic rod shaped *Clostridium welchii* or another of the organisms that produce gas gangrene. The escape of bubbles of gas when pressure is applied over the edges of the wound, and the demonstration of gas in the tissues by x-ray examination are late symptoms of diagnostic value, but symptoms that indicate an advanced process and a grave prognosis.

The treatment is prompt excision of the involved tissue, which often means excision of an entire muscle or group of muscles because the infection tends to progress proximalward and distalward within the substance of a muscle and to remain confined, at first, to the muscle or muscles primarily infected. Sulfadiazine zinc peroxide (Meleney) which furnishes a slow and constant supply of oxygen to the wound area, and serum which is active against *Clostridium welchii* and vibron septicum are all helpful in bringing about arrest of the infectious process. Irradiation of the affected area has been strongly advocated by Kelly. Because gas gangrene is relatively uncommon, even among war wounded and air raid casualties the most effective method of treatment apart from excision of the affected tis-

sues, and the relative value of the methods mentioned are still not definitely determined.

*Chronic undermining ulcers* resulting from infection with the microaerophilic hemolytic streptococcus have been well described and successfully treated by Meleney. He has constantly emphasized careful study of the bacteriological flora and recognition of the causative microaerophilic hemolytic streptococcus, complete excision of the overhanging undermined edges of the ulcer and of sloughs from it, and daily dressings with a cream suspension of active zinc peroxide, applied in such a way that the oxygen is slowly liberated during a period of 24 hours. When the infection is brought under control the extensive open wound is covered with skin grafts.

*Bacterial synergistic gangrene* has also been particularly well described by Meleney. He has emphasized as diagnostic criteria the constantly widening ulcer which forms in the gangrenous skin sloughs, the advancing, violaceous purple or bluish purple indurated border, exquisitely painful and sensitive to pressure, and the constant presence on culture of a microaerophilic nonhemolytic streptococcus in the advancing margin and of a hemolytic staphylococcus in the gangrenous portion. This condition has consistently yielded to Meleney's hands to cauterity or knife excision of the entire indurated margin, clean surgical care and finally covering of the raw surface with skin grafts.

## BURNS

In spite of the many and excellent discussions that have appeared in recent surgical literature with reference to burns it should be emphasized again that burns are large open wounds, and the same principles of treatment apply that have been stressed in the general treatment of wounds—conversion of the contaminated wound into a clean wound, application of an occlusive dressing that provides pressure, and provision for complete rest of the injured part. Siler has focused attention on this method by the apt and concise phrase "primary cleansing, compression and rest" in treatment of burns. There is little argument among surgeons as to the necessity of antiseptics and combatting shock and methods

of doing so are fairly well agreed upon. Unfortunately, there is as yet little agreement concerning the most satisfactory method of local treatment of the burned area.

A primary consideration is conversion of the contaminated wound into a clean wound by the simplest method that does not add further contamination and further injury. That method, in our minds, is not with the aid of chemicals but with simple, nontraumatizing soap and water cleansing carried out with cleanly surgical technique. When it has been accomplished, and loose destroyed tissue lifted or cut away with sterile instruments, the open wound is covered with a nonadherent dressing, such as a single layer of fine meshed gauze saturated with vaseline, that does not fix or coagulate tissue and that, although nonadherent, permits the escape into the outer covering dressing of the exudate, the "white hemorrhage," that escapes from the burned surface until it is arrested by pressure. Compression is provided by sterile gauze, and by mechanics' waste or sea sponges outside the sterile gauze bandaged under moderate tension, preferably with an elastic bandage such as a stockinet. Not only does such compression arrest escape of plasma from the surface, but it checks the escape of serum into the cellular tissue underneath the surface and helps to limit the vital loss of fluid into the deeper tissues that is such an important factor in the production of shock.

The advantages of such a method of treatment are many. (1) It is simple and concluded in one stage. After the dressing is applied a splint is added, if the burn involves an extremity, and the patient left alone. (2) The chances of adding further contamination are reduced to a minimum. (3) The deeper layers of the skin, if still present to furnish a source for regeneration of the skin covering, are not fixed by a chemical coagulant. Expressed a little differently, if only a thin layer of the corium or dermis is left undestroyed by the original injury the few remaining epithelial elements which might furnish a source for reformation of the covering skin are not rendered inert by application of a chemical coagulant. (4) If the effort to convert the contaminated wound into a clean wound is unsuccessful

and infection develops, removal of the dressing to permit recognition of the affected area is a simple procedure. The difficulty of recognizing the exact site of infection under an extensive coagulum and of gaining access to it has disturbed many a surgeon in the care of a severely burned patient. (5) The advantage of providing adequate pressure over the affected area and at the earliest possible moment has been emphasized. A coagulant crust cannot provide the same degree of pressure nor provide pressure promptly. Every surgeon who has employed coagulant dressings recognizes the fact that exudation into the deeper tissues of the burned extremity, not from the burned surface, continues until it is checked by coagulation or by the increasing interstitial pressure in the tissues underneath the burned surface. The shock which is of such concern to the surgeon who is treating burned patients can be reduced, at times averted, by preventing the loss of plasma into the body tissues.

If the patient is seen late, and the burned area has already been covered with grease or ointment the advantage of cleansing the raw surface and applying a dressing which does not coagulate the surface and which can be removed with minimum difficulty is obvious. In such cases, too, the use of a chemotherapeutic agent to combat infection can be of great value. The most helpful method of utilizing the sulfonamides in such cases is receiving serious attention in a number of surgical clinics, but it should be emphasized that it is in patients with large open wounds in whom control of fluid balance may be difficult or impossible at the moment that there lies the greatest danger of rapid absorption, of inadequate elimination and resulting toxemia.

If the patient comes with a frankly infected wound the problem is similar to that of any other infected wound, but aggravated by the extent of the injury, the circulatory damage that has taken place, and the possibility that a virulent infection may be present.

#### REFERENCES

1. ANDERSON, ROGER. *Surg Gyn Obst.*, 1934, 58 639.
2. ANDERSON, WILLIAM. *The Early Treatment of War Wounds*. London: Oxford University Press, 1941.
3. BLAIR, V. P. *Illinois M J*, 1924, 46 249-252.

4. COLERBROOK, L. Proc. R. Soc. M. Lond., 94 34  
343-347
5. FAXON, N. W. and CHURCHILL, E. D. J. Am. M. Ass. 94, 20 385-388.
6. HARR, RONALD. Lancet, Lond., 940, 109.
7. Idem. Canad. Pub. Health J. 940, 3 407-413.
8. Ibid. 940, 3 530-535.
9. JEFFERY, J. S. Edinburgh M. J. 940, 47 7-7
10. KELLY, J. R. Radiology 94 37 43-45.
11. KENNEDY, R. D. Ann. Surg. 94 3 943-954.
12. KERRICK, R. L. Surg. Gyn. Obst. 942, 75 65-69
13. LOCKWOOD, JOHN S. J. Am. M. Ass., 940, 5  
90
14. LOCKWOOD, JOHN S. and LYNCH, HELEN M. J. Am. M. Ass., 940, 14 939-940.
15. LONG, P. H. J. Am. M. Ass. 941, 6 399.
16. LONG, P. H., BLISS, E. A., and OTT, E. Bull. Johns Hopkins Hosp., 94 69 297
17. L. O'NEAL, CHASE J. Am. M. Ass., 935, 3 972-975
18. Idem. Ann. Surg., 94 3 3-7
19. L. O'NEAL, CHASE and HERRICK, CHARLES. Surg. Gyn. Obst. (Internal Abstr. Surg.) 943, 74 571-577
20. LYONS, CHASE and GARD, ROBERT NORTON. Laryngoscope, 942, 50 756-766.
21. MAROW, M. L., and ALLEN, H. B. Am. Surg. 142  
3-444 450
22. McLEARY, F. L. Ann. Surg., 931 94 946-951
23. Idem. Surg. Gyn. Obst., 933 96 819-827
24. Idem. Surgery, 937 169
25. Idem. N. York State J. M., 936, 30 1178-1179
26. OWEN, H. WICKETT Woods and Fracture Spr. Field, Ill. C. C. Thomas, 94
27. P. TAY, D. H. and ROBERTSON, J. P. Lancet, Lond. 941 780-782.
28. PRITCHER, D. B., and SEVIER, C. M. Jr. Am. Surg. 94 3 30-34
29. PULASKI, E. J. McLEARY, F. L. and STURGEON, W. L. C. Surg. Gyn. Obst. 1941, 72 949-950
30. REID, MONT R. N. England J. M., 936, 5 111-114
31. REID, MONT R. and CARTER, B. V. Am. Surg. 941 14 4-18
32. SEARS, DON, P. Surgery 930, 7 0-3.
33. SILVER, V. E. Surg. Gyn. Obst. 942, 72 126-127
34. THURMAN, JOSE. Treatment of War Wounds and Fractures. New York. Paul B. Hoeber 1940
35. TRUSTA, J. and BARNES, J. M. Brit. M. J. 940, 46
36. WELSH, PHILIP D. Ann. Surg. 941, 113 943-944



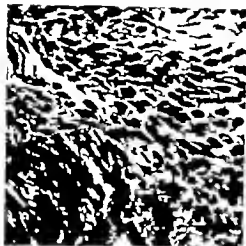


Fig. 4



Fig. 5

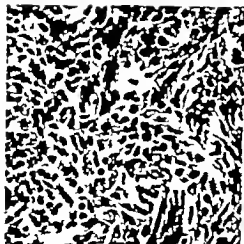


Fig. 6

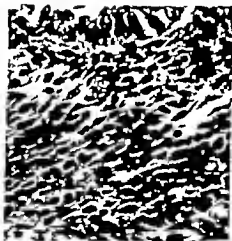


Fig. 7

Fig. 4. Normal endometrium. Zone of transition between myometrium (lower left) and endometrium (upper right). The stroma is dense and compact in the myometrium, fine and delicate in the endometrium (Heidenhain aniline blue stain, X 900).

Fig. 5. Adenomyoma. Intermingling of myometrial and stromal cells. The chief differences are the shape of the cells and the character of the stroma. (Heidenhain aniline blue stain, X 900).

Fig. 6. Adenomyoma. Myometrium (right, endometrium at the left). The transition is so gradual that many cells cannot be classified as belonging to either layer (Heidenhain aniline blue stain, X 900).

Fig. 7. Adenomyoma. The delicate contractile stroma of "smooth" cells can readily be seen. An endometrial gland is seen at the upper edge. The transition from the myometrium can be seen at the lower edge (Heidenhain aniline blue stain, X 900).

# ADENOMYOSIS OF THE UTERUS

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**A**DENOMYOSIS may be defined as the heterotopic occurrence of islands of endometrium within the myometrium or uterine wall. It is distinct from endometriosis in which disease the heterotopic endometrium is situated outside of the uterus.

Under the title of "Ueber Uterusdruesenneubildung im Uterus," adenomyosis was first described by Rokitansky in 1860. German and Viennese pathologists and gynecologists, particularly Frankl, first consistently employed the term adenomyosis. In an article published in 1932 Frankl (13) states that he was first to recognize the condition as an entity and to describe it as such, microscopically and otherwise, in 1912. Much of the literature has been confusing, with overlapping and interchanging of the terms adenomyosis, adenomyoma, and endometriosis. The important contributions to the subject in general by Babes in 1881, Cullen (6) in 1908 and Sampson (30, 31) in 1921 and 1922 must be accorded full recognition. In 1896 von Recklinghausen published an article on the subject. In 1914 Cullen (7) reported 70 cases of adenomyoma of the uterus collected from the gynecological clinic at Johns Hopkins Hospital. It seems quite likely that the majority of the cases reported at that time and since as adenomyoma were really adenomyosis.

In addition to the various terms employed as synonyms for endometriosis, adenomyosis has been referred to as adenomyoma, adenomyomatosis, internal and external uterine endometriosis, von Recklinghausen's disease, adenometritis, adenomyositis, and adenomyometritis, the last three being particularly inappropriate. It might be suggested that if adenomyosis were not the term employed, uterine or intrauterine endometriosis would probably be of second preference. While adenomyosis is frequently included under endometriosis, it is usually not difficult for the interested reader or listener to distinguish the two lesions. Internal and external endometriosis are employed, the former meaning adenomyosis of the uterus and the latter meaning extrauterine endo-

metriosis, and to make the subject more confusing, external endometriosis is occasionally used to mean adenomyosis of the outer portion of the uterine wall.

The approach to this subject has been rendered difficult because of the confusion in terminology and the failure to distinguish precisely between adenomyosis, adenomyoma, and endometriosis in the earlier literature dealing with this disease. The more recent literature has by no means clarified the subject. The greatest confusion concerns adenomyosis and adenomyoma. To some extent the term adenomyoma has been used synonymously with adenomyosis, the former being widely used to connote what we now prefer to call the latter. The two lesions are distinctly different and yet in the earlier reports discrete encapsulated myomatous tumors containing glands were described. One is perplexed, however, by the apparent frequency with which these tumors were encountered at one time and their comparative rareness today. It must be realized that even in present day literature and medical terminology, adenomyoma actually means adenomyosis.

That adenomyosis is a common lesion has often been stated but its incidence varies considerably in the experience of various observers. Lewinski reports the incidence as 53.5 per cent of uteri removed at necropsy and considers adenomyosis, especially adenomyosis interna, as practically a physiological condition. Fallas and Rosenbloom collected 260 cases of endometriosis among their gynecological operations, an incidence of 1.62 per cent. Of their 260 cases, 49.6 per cent were internal endometriosis (adenomyosis). Von Geldern found that in one thousand consecutive pelvic operations at Stanford University Hospital there were 86 cases of uterine adenomyoma and 54 of other types of intrapelvic endometriosis. It may be assumed that he means adenomyosis instead of adenomyoma. Counsellor does not separate adenomyosis from endometriosis but states that, of 884 cases of the latter, the lesion was in the uterus in 69.9 per cent. Dougal makes the statement that for every one hundred "fibroids" there are 6 cases of internal and 25 of external endometriosis. Dannreuther found that of 115 cases of pelvic endometriosis, 39 were adenomyosis and 10 were adenomyoma. Dreyfuss reports an incidence of

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Part of the material in this paper was submitted by one of us (JHB) in partial fulfillment of the requirements for the degree of Master of Science in Surgery, Wayne University College of Medicine, Detroit.



12.4 per cent of endometriosis and adenomyosis combined, 70 per cent of which was adenomyosis, in 1,807 uteri removed. Cross-sectional experience would seem to indicate that adenomyosis is three times as prevalent as endometriosis. Frankl (14) states that the frequency of uterine adenomyosis is 8 per cent that of myomas.

To evaluate the experiences of various authors one should know how their observations were made. If the uteri constituting the material were examined properly, systematically and carefully, if the study was planned in advance and executed purposefully with uniform data recorded in each case for further analysis, or whether the study was made in retrospect. An exact and proper pathological examination of each uterus is imperative. Tissue blocks must be cut perpendicular to the endometrial surface and must not be taken from the uterine cornua. Failure to observe this precaution might explain the extremely high incidence of adenomyosis reported by some authors. Obviously the frequency with which the lesion is found will depend upon the number of sections examined in each case because the diagnostic areas may be so sparsely or unevenly distributed as to be easily missed if too few sections are depended upon. A fair ratio should be maintained between the number of blocks taken for examination and the weight of the uterus. Further one should know what criteria were employed in establishing a diagnosis of adenomyosis. By definition, adenomyosis consists of extension of the endometrium into the myometrium, but is it to be assumed that the line of demarcation between the two normally is always a sharp even one? Are slight invaginations, so often seen, instances of adenomyosis representing edges of deeper invaginations demonstrable by serial sectioning? Where must one draw the line between the normal and the pathological? These questions and others can be answered only arbitrarily.

From various reports it is apparent that the majority of cases of adenomyosis occurs during the latter part of and somewhat beyond the period of reproductive life. The commonest decade is the fifth. Skamnakis found that in his series of cases 53.6 per cent were in the fifth decade and that 90.6 per cent occurred between the ages of 30 and 60 years. Dreyfuss stated that 90 per cent of his patients with adenomyosis were over 35 years of age, 7 per cent were over 40 and the average age was 46 years, and he pointed out that this was distinctly a disease of the second half of the generative period, many patients being postclimacteric. Of patients with endometriosis on the other hand he found that 30 per cent were under 30

years, 54 per cent under 35, and the average was 33. Frankl (15) however found that of 21 patients with adenomyosis 10 were in the 4th, 11 in the fifth and 15 in the sixth decade. He states that "we may consider adenomyosis a disease which occurs in the preclimacteric age group before menarche, and probably never after menopause, although it may become manifest several years after the menopause."

#### PATHOLOGY

In uncomplicated adenomyosis the uterus is usually from slightly to greatly enlarged due to thickening of the uterine wall, chiefly the result of associated myometrial hyperplasia. This thickening is usually diffuse and symmetrical, but occasionally the enlargement is irregular and asymmetrical due to an irregular distribution of the bulk of aberrant endometrium. Examination of the cut surface reveals a trabeculated whorl-like appearance and while there are no circumscribed nodules, there are indefinite poorly circumscribed areas consisting chiefly of concentrically hyperplastic myometrium about the endometrial islands. Occasionally there are cysts in the centers of these nodules which are usually but a few millimeters in diameter but which, in rare instances, are from one to several centimeters in diameter. Occasionally these cysts contain blood but usually not. In some cases there are adhesions between the uterus and other pelvic structures due to associated peritoneal endometriosis or to a serosal inflammatory reaction subsequent to subperitoneally located islands of endometrium in the uterine wall. The myometrium is generally firm, sometimes hard.

Microscopically the important feature is the abnormal presence of endometrium within the myometrium. This may be in the form of irregular islands or strands which are usually perpendicular to the endometrial surface. The inner half of the uterine wall is most frequently and most extensively involved. The endometrial glands are surrounded by cytogenic stroma which, when present ectopically without association with glands, should provide the diagnosis of adenomyosis. The cyclic menstrual changes of the normal endometrium are faithfully reproduced in the aberrant endometrium, but actual bleeding into the lumens of the glands rarely occurs (Dockerty). The absence of blood in these glands or cysts must be interpreted to mean that the glands communicate with the uterine canal and their contents are permitted to empty or drain into the canal. This communication doubtless often exists, but the absence of blood in these misplaced glands is probably due to the fact that hemorrhage into the

glands does not occur. Abnormal changes in the endometrium lining the uterine canal do not occur in adenomyosis. Invasion of the cervix by adenomyotic glands apparently does not occur.

**Associated lesions.** Rockstroh reported the presence of myoma of the uterus in 70 per cent of the cases of adenomyosis which he studied, Frankl (16), 30.7 per cent, and Adler, 40 per cent. In a series of 99 cases of adenomyosis Skamnakis found some type of uterine or adnexal disease in all but 8. The lesion most commonly found in association with adenomyosis was uterine myoma, which was present in 53.8 per cent of the cases. He did not record the presence of myometrial hyperplasia. Skamnakis concluded that when carcinoma of the uterus was present, the concurrence of the two lesions was merely a coincidence, even if the neoplasm was an adenocarcinoma of the corpus uteri. This agrees with Meyer's viewpoint. The complication of carcinoma of the uterus in cases of adenomyosis "interna" has been recorded by Frankl as 2.8 per cent, by Rockstroh as 2.7 per cent, and by Skamnakis as 6 per cent. Dreyfuss found myomas present in 62 of his cases of adenomyosis, myometrial hyperplasia in 44, both in 40, and atrophy of the myometrium in 7.

Witherspoon stresses the theory of estrogenic principle in etiology, believing that hormonal stimulation causes all overgrowths of endometrium and myometrium, including neoplasms. This would explain the frequent coexistence of uterine myomas, adenomyosis and both myometrial and endometrial hyperplasia.

#### PATHOGENESIS AND HISTOGENESIS

The following theories of origin of adenomyosis, and seemingly adenomyoma as well, have been postulated by students of the subject:

1 *Direct invasion of myometrium by endometrium.* The actual mechanism of such a phenomenon is not clear, but it may be suggested that normally the myometrium exerts a certain physiological pressure against invasion by the endometrium with which it is in direct and intimal contact, and the loss, absence, or diminution of such pressure may permit invasion or intermingling. Some such biological pressure must prevent the encroachment of epithelium and connective tissue throughout the body. Both Cullen (6) and Frankl (14) have championed the invasion theory, and apparently it has been applied with equal facility to adenomyoma, a process more difficult to understand. The stroma of the islands of adenomyosis interna is presumably derived from the mucous membrane, preparing the way for the glands which are to follow in its track (13).

2 The islands of glandular epithelium represent misplaced remnants of muellerian duct epithelium (Cullen, 6).

3 The epithelium originates from mesonephric tissue (wolffian duct) (von Recklinghausen, Pick, Pfannenstiel, and others).

4 It is the result of fetal budding of the epithelium.

5 The condition represents misplaced islands of fetal mucosa.

6 The condition results from misplacement of gland tissue.

7 It is caused by invasion of the myometrium by gland alveoli during inflammation (Chiari). This may be considered under item 1.

8 It originates from the peritoneum by further differentiation or metaplasia of mesothelium (Ivanoff, Meyer, Witherspoon, Meigs, Holmstrom).

9 Migratory or metastatic theory (Sampson, 32, in 1927). Endometrium is carried through blood and lymph vessels and becomes deposited in the myometrium (Bertner).

Holmstrom distinguishes between adenomyosis uteri *interna*, in which he believes the glandular tissue arises from the endometrium, *externa* which occurs on or beneath the serous surface from (a) endometrial transplants or (b) metaplasia from serosal cells, and a third or intermediate type arising from aberrant parts of muellerian duct.

Over a 10 year period in the Alexander Blain Hospital there were 73 cases of adenomyosis of the uterus, representing an incidence of 10.7 per cent of all uteri removed. These 73 cases were analyzed as to pathological findings.

The gland areas were diffusely distributed throughout the myometrium in 24 cases, in the inner two thirds only in 49, and in the outer one-third only in 3. In 5 additional cases only a shallow submucous zone was involved. The subserous zone was involved in but 2 cases and in 1 of these there was serosal endometriosis. In 13 cases microscopic cysts were present. Some of these were of sufficient size to be seen upon microscopic examination if carefully looked for, but no gross cysts were present. In 2 cases the glands contained some blood. Contrary to the observations of Dockerty, the glands of the adenomyotic areas in the material examined did not undergo the same cyclic changes as did the surface epithelium. Stromal proliferation apparently did occur in the latter two-thirds of the intermenstrual cycle due to progesterone influence, but changes in the epithelial cells appeared to be negligible. The adenomyotic glands more closely resembled those of the stratum basalis and did not participate to any extent in the cyclic change.

The lumens of the adenomyotic glands in the inner third of the uterine wall invariably communicated with the surface endometrium and presumably with the uterine canal, as could be demonstrated by serial sectioning. Those in the outer wall did not.

In a distinct minority of cases there was localized hyperplasia of the myometrium about the adenomyotic areas. This in some instances produces a gross nodularity and might lead to a diagnosis of adenomyoma, although the nodules are not actually neoplastic. It is conceivable that adenomyomas could be produced in this manner.

In *Gray's Anatomy* (22) the statement is made that the weight of the normal previously pregnant uterus is 42 grams. Of 51 uteri in this series, whose weights were available, 46 weighed between 50 and 150 grams, the average being 124.25 grams.

The endometrial stroma is a somewhat embryonic type of tissue, generally considered to be connective tissue, from which the endometrial glands are presumably derived; therefore the name cytotropic stroma. These cells are recognized as being endowed with a peculiar instability. Goodall states: "The stromal cell of the ovary is a very versatile structure. It now turns out that the stromal cell of the uterus runs it a close second. It is the precursor of the glandular structures of the uterine mucosa. In the past we have given too much attention to the glandular elements and not enough to the stromal cells."

Various differential tissue stains were employed in our series of cases to distinguish sharply between endometrial stromal cells and the non-striated muscle cells of the myometrium. It was found that Heidenhain's modification of Mallory's aniline blue stain, which utilizes azocarmine in stead of acid fastness, furnished the sharpest differentiation, staining both cytoplasm and nuclei of muscle cells brilliant red, and both cytoplasm and nuclei of connective tissue cells and collagen deep blue. The following features were strikingly apparent:

1. In both the normal endometrium and adenomyotic islands, the stromal cells of the endometrium and the muscle cells of the myometrium possessed identical staining reactions.

2. A gradual transition between myometrial and endometrial cells occurs.

3. A zone between the two layers exists in which it is impossible to determine if the cells belong to the myometrium or endometrium.

4. Deeper in the endometrium the shape of the cells becomes altered, the cells becoming shorter and more plump, the staining characteristics remaining the same.

5. Between the interstitial cells of the endometrium there exists a fine delicate stroma, which stains blue in contrast to the red-stained interstitial (stromal) cells. This is identical to the stroma of the normal myometrium.

6. This blue-staining, reticulum-like matrix is the true stroma of the endometrium.

7. The cells of the endometrium usually refer to as the interstitial cells (cytotropic stroma) are really parenchymal cells, as much so as the smooth muscle cells of the myometrium to which they are genetically related.

We wish to advance the theory that by a process of dedifferentiation or metaplasia, probably the former, less mature but more highly specialized cells are produced, and that these cells possess the potentiality to differentiate into epithelial cells which form endometrial glands. This process is similar to the differentiation of fibroblasts by osteoblasts and chondroblasts and is in accord with the generally accepted theory that mesothelial cells of the peritoneum differentiate into endometrial stromal cells giving rise to endometriosis. Other comparable examples could easily be found.

Dedifferentiation, or loss of differentiation of cells, is commonly encountered in the field of oncology and is the mechanism by which sarcomatous neoplastic cells are derived from mature cells, notably surface epithelial cells, and also observed in neoplasms which acquire a greater degree of anaplasia. The same mechanism explains the transition from hyperplasia to neoplasia in the development of tumors. In this special phase, of course, the resultant cells are not neoplastic, but the analogy is important.

The uterine wall is composed of three layers: mucosa, muscularis, and serosa. There is no serosa. In fact there is no sharp line of demarcation between the endometrium and myometrium, but rather the one merges gradually with the other so that it is difficult to determine exactly at the border-line just which cells belong to the myometrium and which to the endometrium. In many instances the zone of contact between the two layers is represented by a fairly even line, but even in many other instances the line is normally uneven with shallow indentations or invaginations of endometrium into the myometrium. This also constitutes a practical difficulty in dissection of a slight degree of adenomyosis from a normal but uneven line of contact.

The entire uterus is derived from the mesoderm, and in the uterus epithelial, connective tissue and muscle cells have a common origin. In the congenital tract the strict specificity of cells, which is commonly believed to characterize cells derived

rom the ectoderm and endoderm, does not seem to exist. Here there is less stability as to cell type and a greater tendency for transition from one cell type to another which is well reflected in neoplasms of the uterus and ovary.

If it may be granted that a transition from myometrial to endometrial stroma cells is possible, then it seems reasonable to suppose that the tendency toward this transition is greater in that portion of the myometrium which is adjacent to the endometrium, and that the tendency decreases proportionately as the distance from the endometrium is increased. This would explain the preponderance of adenomyosis in the inner half or third of the uterine wall.

That the cells of the endometrial stroma represent a less mature type of non-striped muscle cell normally composing the myometrium is consistent with the fact that some leiomyosarcomas of the uterus are composed of cells almost identical as to size, shape and staining reaction to those normally forming the endometrial stroma.

That in adenomyosis the stromal cells are formed first and the epithelial cells second is borne out by the fact that in this lesion small islands of stromal cells are encountered which by serial sectioning can be shown to be unaccompanied by or unassociated with gland formation.

#### EVALUATION OF STUDY

The confusion in nomenclature and the promiscuous overlapping and intermingling of distinct and separate lesions renders any attempt to evaluate the literature as to incidence and other data quite futile.

Adenomyosis has no appropriate synonym. As a pathological entity it is distinctly different from adenomyoma and endometriosis.

Whether the lesion represents a minor deviation from the physiological normal or whether it is



Fig 1 Typical adenomyosis involving the inner half of the wall. The islands of endometrium in the center actually communicate with the mucosa.  $\times 75$

actually a disease is debatable. Mild types are separated with difficulty, but the more advanced or severe types are obviously pathological. This can be said of many lesions.

In a strict sense, endometriosis does not involve the myometrium with the exception of the shallow subseral invasion of endometriosis of the uterine peritoneum.

The difference between adenomyosis and endometriosis is reflected in the age incidence of patients with the two diseases. In the former women in late and middle life are affected, whereas the latter is a disease of women during their most productive years. The two lesions are rarely associated and occupy distinctly different anatomic sites.

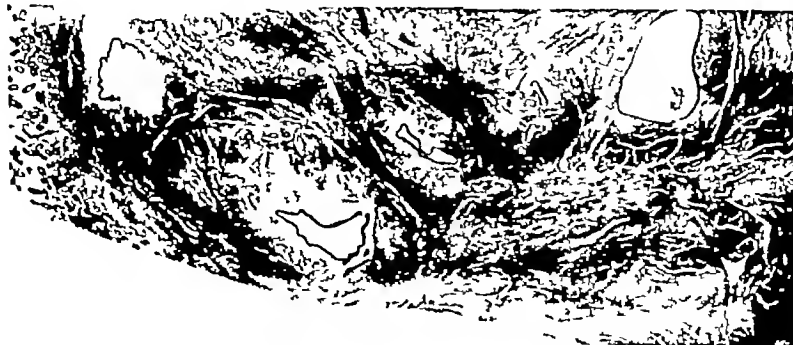


Fig 2 Diffuse adenomyosis with cysts of microscopic size.  $\times 66$

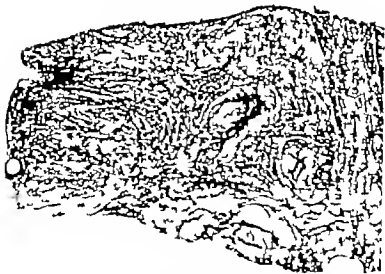


Fig. 3. Adenomyosis with trophy of endometrium. Zone of Stromyosarcoma hyperplasia about the endometrial islands has been called "adenomyoma." X75.

In adenomyosis the islands of endometrial glands are more numerous and more frequently situated in the inner half of the uterine wall and often communicate with the mucosal layer. This suggests that the mechanism of production of the lesion is direct invasion from the endometrium. This does not, however, explain the existence of islands of endometrium farther out in the uterine wall which apparently do not communicate with the mucosa. From the standpoint of histology, morphology, and embryogenesis it seems more correct to believe that the endometrial stroma (interstitial cells) is derived by process of dedifferentiation from the myometrium. These cells may be either non-striated muscle cells or connective tissue cells, a transition from the former to the latter being not impossible in the urogenital tract. This would quite satisfactorily explain the development of endometrial islands anywhere in the uterine wall and would also account for their greater prevalence in the inner zone, inasmuch as normally the potentiality for myometrium to change into the endometrial stroma is greatest at the endometrial junction.

Some of the endometrial islands are composed only of stromal cells, a situation which approaches interstitial endometriosis described by Goodall. Such a distinction from adenomyosis is probably not warranted because whether glands are present or not is really not important, the assumption being, and probably correctly so, that the endo-

metrial stroma (cytogenic stroma) is composed of immature cells capable of differentiation into glands. This differentiation may or may not have occurred.

The opinion has often been expressed that adenomyosis, as well as other pathological proliferations and hyperplasias of uterine tissue, are dependent upon ovarian influence. This seems to be a reasonable hypothesis, not easily contradicted, and supported by the fact that adenomyosis is often associated with hyperplasia of the endometrium and myomas of the uterus.

To a limited extent the misplaced islands of endometrium in the uterine wall undergo cyclic menstrual changes similar to those of the normal endometrium. Usually, however, the ectopic endometrium possesses greater similarity cytologically to the stratum basalis of the normal endometrium, participating only slightly or moderately in the typical cyclic changes.

Adenomyosis is only rarely associated with leiomyoma or sarcoma of the uterus and when so, is usually incidental. Adenomyosis can be definitely said not to be a potentially malignant lesion.

We believe that we have produced proof that the cytogenic stroma of the normal endometrium is derived from the non-striated muscle cells of the myometrium by process of dedifferentiation, the cells thus produced being less mature and possessing a greater capacity or potentiality for differentiation than the cells they develop.

Adenomyosis is the result of spontaneous generation of endometrial stromal or interstitial cells from and within the myometrium, this tendency being greatest near the normal endometrium and decreasing toward the serosa

The stromal or interstitial cells thus produced differentiate later to form the gland cells of the endometrium

The so-called stromal or interstitial cells are really parenchymal cells and possess a finely distributed true stroma

## REFERENCES

- 1 ADLER, L. In Halban Seitz, *Biologie und Pathologie des Weibes*, vol 4, p 160 Berlin Urban & Schwarzenberg, 1928
- 2 BABES, V. *Orv hetil*, 1881, 30 1205-1210
- 3 BERTNER, C W. *South M J*, 1939, 32 989-994
- 4 CHIARI, H. In Lynch, F W, *Pelvic Neoplasms*, p 165 New York D Appleton Century Co, 1926
- 5 COUNSELLOR, VIRGIL S. *Am J Obst*, 1938, 36 877-888
- 6 CULLEN, T S. *Adenomyoma of the Uterus* Philadelphia W B Saunders Co, 1908
- 7 Idem *J Am M Ass*, 1914, 62 835-839
- 8 DANNREUTHER, WALTER T. *Am J Obst*, 1941, 41 461-474
- 9 DOCKERTY, M B. Quoted by Waugh, John, *M J Lancet*, 1941, 41 24-27
- 10 DOUGAL, DANIEL. *Am J Obst*, 1938, 35 373-386
- 11 DREYFUSS, MARTIN L. *Am J Obst*, 1940, 39 95-99
- 12 FALLAS, ROY, and ROSENBLOOM, GORDON. *Am J Obst*, 1940, 39 964-975
- 13 FRANKL, OSKAR. *Irish J M Sc*, 6th series, June 1932, pp 303-307
- 14 Idem *Zbl Gyn*, 1932, 56 902-927
- 15 Idem *Zschr Geburtsh Gyn*, 1937, 115 1-17
- 16 Idem *Am J Obst*, 1925, 10 680-684
- 17 GELDERN, HANS VON. *West J Surg*, 1940, 48 154-168
- 18 GOODALL, JAMES R. *Tr Am Ass Obst*, 1937, 50 192-230
- 19 HOLMSTROM, E G. *Am J Obst*, 1941, 41 139-142
- 20 IVANOFF, N S. *Vrach (St Petersburg)*, 1897, 18 1419-1445, also *Mschr Geburtsh Gyn*, 1898, 7 295-300
- 21 LEWINSKI, W. Quoted by Zaleski, W. *Zbl Gyn*, 1936, 60 1046-1050
- 22 LEWIS, W H. *Gray's Anatomy*, 23d ed, p 1251 Philadelphia Lea & Febiger, 1936
- 23 MEIGS, JOE V. *Ann Surg*, 1941, 114 866-874
- 24 MEYER, ROBERT. In Hencke Lubarsch, *Handbuch der speziellen pathologischen Anatomie und Histologie*, vol 7, part 1, p 249 Berlin Julius Springer, 1930
- 25 PFANNENSTIEL, J. *Ueber Adenomyome des Genitalstrangs* *Verh Deut Ges Gyn*, 1897
- 26 PICK, L. *Arch Gyn*, 1897, 54 117
- 27 RECKLINGHAUSEN, C VON. *Die Adenomyome der Uterus- und Tubenwandung* Berlin A Hirschwald, 1896
- 28 ROCKSTROH, H. *Zbl Gyn*, 1936, 110 550-559
- 29 ROKITANSKY, C F VON. *Zschr Gesellsch Arzte*, Wien, 1860
- 30 SAMPSON, JOHN A. *Tr Am Gyn Soc*, 1921, 46 162-241
- 31 Idem *Am J Obst*, 1922, 4 451-512
- 32 Idem *Am J Path*, 1927, 3 93-109
- 33 SKAMNAKIS, STELLIO N. *Zbl Gyn*, 1938, 62 414-423
- 34 WITHERSPOON, J. *Thornwell Surg Gyn Obst*, 1935, 61 743-750

# THE RAPID PREPARATION OF EYESOCKETS

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THE majority of war injuries requiring eye enucleation that have been admitted to Brenthurst Military Hospital have not been straightforward in that either conjunctiva or bone framework has been lost. This condition leads to an obliteration of the sulcus necessary to hold an artificial eye. In order to provide suitable socket, therefore, some form of plastic operation has to be performed.

The usual approach to this problem has usually entailed the complete removal of the conjunctiva and an Ollier Thiersch graft replacement of the raw bed. This operation has been performed by making a mold of the desired socket in gutta-percha, covering it with a Thiersch graft, and embedding it in the socket by performing a complete tarsorrhaphy.

Two complications militate against perfect results in a fair percentage of cases (1) the invariable tendency for graft contracture and (2) sepsis.

The tendency for graft contracture lasts several months and because of this fact the mold has to be kept in for a considerable period, the average being about 3 months. As the contracture tension is uniformly toward the center of the mold from all directions, there is a distinct risk that the gutta-percha may burst the bonds of the tarsorrhaphy and slowly extrude from the socket. The risk is, of course, increased if sepsis intervenes. It does, in spite of all precautions, in certain percentage of cases. It is therefore obvious that this type of case has to be under close

supervision by the plastic surgeon for a period of about 3 months and sometimes longer.

It is the purpose of this paper to present a method of socket preparation whereby graft contracture is not a disadvantage, sepsis is controlled, and the period of hospitalization is brought down from months to days.

## METHOD

The prosthesis used is a transparent acrylic the size and shape of an artificial eye. It can be modified as required by the addition of stent composition. The acrylic is parcelled in steel tubes set at an angle with the apex placed posteriorly and the divergent arms, which stand out for a distance of about  $\frac{1}{2}$  inch, placed anteriorly (Fig. 1).

The bed for the graft is prepared by carrying incisions from immediately behind the temples to meet at the outer and inner canthi. Then a complete oval trough is made, the vertical depth being half the vertical height of the prosthesis.

The prosthesis is now covered by Thiersch graft which has been split posteriorly to allow for drainage. The whole is now kept in position by performing a medium tarsorrhaphy between the divergent arms of the steel drainage tubes.

It will be noticed that the conjunctiva is not disturbed but is allowed to retract toward the back of the orbit. This area is kept free of discharge by constant saline irrigation, the fluid being introduced by a chip syringe through one of the drainage tubes, the effluent passing out through the other. The graft is, of course, not interfered with in any way.



Fig. 1. The acrylic eye.



Fig. 2. Graft on acrylic.



Fig. 3. Graft on acrylic.

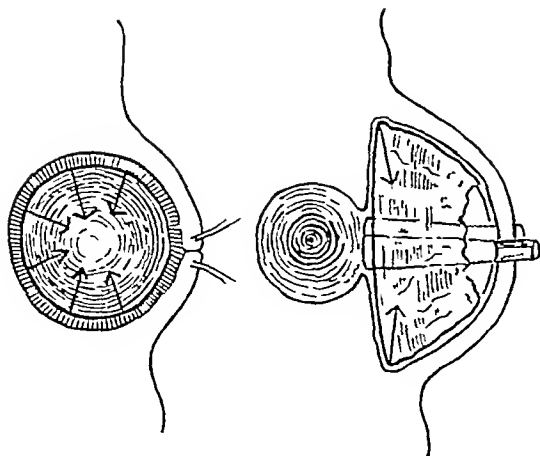


Fig 4 Left, Tension, accomplished by the old method

Fig 5 Tension, accomplished by the Brenthurst method

The graft tension in this case does not tend to close down toward the center of a sphere but toward the center of a circle, therefore the tendency is to grip the prosthesis more firmly but not to extrude it (Figs 4 and 5)

When this procedure is followed the plastic prosthesis can be removed in 5 days, leaving a grafted socket which can immediately accommodate an artificial eye



Fig 6 Left, Photograph showing the prepared socket

Fig 7 Photograph showing the artificial eye in position

After another few days of retention at the plastic center so that the patient may learn to carry out the correct orbital hygiene, he is discharged with strict injunctions that the artificial eye must be worn day and night for at least 4 months and is to be removed only for the purpose of irrigating his socket

#### SUMMARY

1 A new method of eyesocket preparation is described

2 The period of hospitalization and after care is brought down from a period of a few months to a few days

This paper is published with the kind permission of Colonel I W Brebner, O C Brenthurst, and Brigadier Sir Edward Thornton, D G M S, South African Forces



# INITIS PLASTICA TYPE OF CARCINOMA

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**E**VER since the recognition of the contracted or "leather bottle stomach" and particularly since Brinton's classical description of this disease which he named "initis plastica," an extensive literature on the nature of this lesion has accumulated. As a matter of fact Howard, who reviewed the literature up to 1933, stated that there were 42 terms coined by various authors as the most appropriate names for this entity. The many different names given to this condition serve as an index of the multiplicity of the views held regarding this disease. Though there are still opinions in favor of a specific or nonspecific inflammation as the principal etiological agent producing initis plastica, it seems clear that more and more evidence is being brought forward in favor of its neoplastic nature.

In the following report the results of a study of 26 instances of so called initis plastica are given. This study was undertaken, not so much for the purpose of clarifying the concept of initis plastica since this has been attempted often previously but rather to see whether investigation of a large amount of autopsy material would disclose diseases other than carcinomas which sometimes cause initis plastica. It was also thought that it might be of interest to study the metastases, whether or not the initis plastica type of carcinoma varies from other carcinomas in the stomach as to the types and locations of metastases, and whether or not there is any difference in survival periods. Because of the fact that autopsy material was exclusively used for this study a comparison could easily be made between the duration of the disease and autopsy findings, in patients with initis plastica carcinoma and in patients with other carcinomas. Only the more pertinent references are given for more complete literature see Lyte, and also Howard.

## MATERIAL STUDIED

This study deals with the examination of 26 patients or records of these patients, showing, either at operation or at autopsy, initis plastica

type of carcinoma. Only the surgical patients who subsequently died and came to autopsy were included in this study. The clinical records and autopsy findings of 40 patients with other types of gastric carcinoma were studied for comparison. Since the latter were observed during the same period as the former the relative incidence of the initis plastica type of carcinoma, as compared with the incidence of the other types of carcinoma of the stomach, could be obtained. Two patients of initis plastica type of carcinoma of the rectum and of the descending colon close to the splenic flexure and 2 of the gall bladder were also included in this study. At autopsy special attention was given to the field of operation for possible evidence of recurrences and to sites of metastases. In instances in which an operation was not performed careful attention was given to the anatomic skeleton of the stomach. Since frequently the bony skeleton could not be examined, metastases in these structures were noted only by roentgenograms. Complete histological studies were made in every instance for the special purpose of establishing a clear-cut histological picture of the changes in the stomach which eventually might aid in the estimation of the prognosis.

It is not the purpose of this communication to analyze clinically these patients with the initis plastica type of carcinoma. Only a few data can be mentioned. Among the 26 patients, 20 were male and 6 were female. The youngest were 24 and 3 years old, and the oldest were 65 years of age. The early symptoms are not considered and it seemed that sensation of fullness in the stomach was most commonly present. The short time interval between the onset of the symptoms and death of the patients who did not submit to surgical procedure is significant. Among such patients, the longest interval was 35 months, among 4, it was 1 year, among the others it was 8 months, 3 months, 9 weeks, 6 weeks, 5 weeks, and 3 weeks, respectively. Three patients came to the hospital in conditions which did not permit operation. Among 40 patients with miscellaneous types of carcinoma of the stomach observed during the same period, 15 died without operation. The time interval be-

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Aided by grant from the Isaac and Kate Meyer Fund, and the Michael Reese Research Foundation.

\*W. are included in the surgical department for the use of the records of these patients.



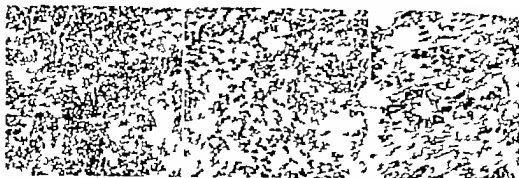


Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1. Note the presence of many nuclei resembling those of large lymphocytes. (Iron hematoxylin-eosin preparation, X 55.)

Fig. 2. Field similar to that shown in Figure 1. The

large dark nuclei are obviously nuclei of tumor cells. (Iron hematoxylin-eosin preparation, X 55.)

Fig. 3. Note the miniature glandular structures. (For hematoxylin-eosin preparation, X 80.)

nized throughout the mucosa. On section the wall of the stomach was found to be greatly thickened. Cross sections often measured 1.5 to 2 centimeters. The lesion often extended in the form of whitish filaments into the muscularis, the filaments actually forming a rough network which again was crossed by fine interlacing fibers which often produced a bistrato architecture with the uninvolved musculature presenting pinkish, glistening inclusions.

The histological elements in the sections of the stomach varied widely. However when enough sections were studied it became clear that similar elements were present in every instance. These were encountered so consistently that it had to be conceded that, from the histological picture alone—without reference to the gross observation

—the correct diagnosis could be established. Most of the sections showed as the outstanding lesion, new formation of connective tissue fibers which often were hyalinized, and extended throughout the entire wall of the stomach and often entered the muscularis. Along the fibers, characteristic of chronic inflammation were also abundant. Large endothelial leucocytes seemed to be the most frequently encountered type of cell. Many lymphocytes and eosinophilic leucocytes were constantly present and plasma cells were common. Polymorphonuclear leucocytes were relatively rare, though in the vicinity of superficial ulcers they were quite frequent. It must be pointed out that lymphocytes were also in a perivascular position. The arteries, particularly the larger ones, showed varying degrees of lesion

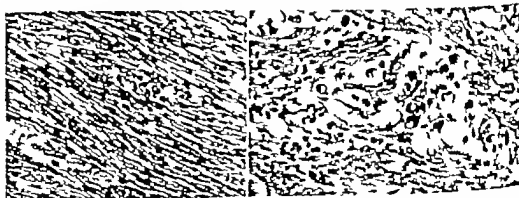


Fig. 4.

Fig. 5.

Fig. 4. Note slight ring shaped tumor cells and dark nuclei of other tumor cells, also marked new formation of connective tissue. (Iron hematoxylin-eosin preparation, X 55.)

Fig. 5. Note the slight ring shaped tumor cells and darkly stained nuclei of tumor cells. (Iron hematoxylin-eosin preparation, X 80.)

cells the glandular structures and the lining tumor cells may either not be recognizable at all or be present singly or in small groups, the other—the signet ring cell mucinous carcinoma, characterized by well preserved mucin secreting cells with basophilic or clear cytoplasm and crescent shaped, compressed nuclei situated at the base of the cell. Signet ring shaped tumor cells were present in every case in this series. Similar cells were also present in many instances of linitis plastica type of carcinoma described in the literature, particularly those studies done more recently by Dixon and Stevens, Chiray and Albot, Monserrat, Premoli, and Riveros. Thus, it seems that the linitis plastica type of carcinoma is primarily an adenocarcinoma in which individual glandular structures are present in diminutive sizes, the individual cells early breaking loose from the acini but still retaining their ability to produce mucin. The 3d type of tumor cell characterized by the presence of hyperchromatic, irregularly shaped nuclei, may be explained by the assumption that after the individual mucin secreting lining cells have become separated from the acini over a certain period of time, they stop producing mucin and the nuclei assume the bizarre form, whereas the cytoplasm is retracted around the nuclei and thus becomes hardly visible.

There are instances of signet ring cell types of mucinous carcinoma of the breast on record, in which the tumor had produced a number of metastases, particularly in the ovaries. Jørgensen termed his type of breast tumor "cancer of the breast with metastases resembling linitis plastica." There was metastasis to the rectovaginal septum. Among the 26 cases in this series, there were 6 females, 3 of whom had metastases to the ovaries and a 4th had metastasis to the pouch of Douglas. Among the 40 control patients showing various other types of gastric cancer, there were also 6 females of whom only 1 had metastasis to the ovary. From this relatively small series, and from certain somewhat similar tumors in other organs, it seems that a tumor containing signet ring shaped tumor cells is more likely to produce metastasis in the ovary than are other tumors. Monserrat very recently again drew attention to the ovaries as sites of metastases from a linitis plastica type of carcinoma of the stomach.

*Clinical findings.* From the clinical point of view the linitis plastica type of carcinoma also seems to behave somewhat differently from other gastric cancers. Clinical symptoms appear late and when patients reach the operating table, a laparotomy often shows an immovable stomach with peritoneal metastases. It is also noteworthy

that the longest survival period following operation was only 3 months, and that among 11 patients it was 11 days or less. This short survival period definitely indicates that these patients were submitted to the surgical procedure as the last resort. Eight of these 11 patients were found to be inoperable on exploration, 5 of these 11 patients died from bronchopneumonia, while 3 showed abscess formations. The pneumonia was obviously an aspiration pneumonia. It seems that because of some obstruction and regurgitation of food, these patients developed aspiration pneumonia and, some of them at least, were operated upon because of intestinal obstruction while they had the pneumonia. This fact may also explain their rapid deaths. Unlike other gastric cancers, the linitis plastica type does not produce a single tumor which causes obstruction or is readily diagnosed by roentgen examination, but produces a diffuse lesion in the stomach. This may explain why the symptoms appear late in the course of the disease.

That linitis plastica type of carcinoma of the stomach constitutes a special form of carcinoma may also be indicated by its metastases. In only 3 out of 26 instances was the liver involved, while in the control group of 40 miscellaneous gastric cancers, the liver showed metastases 19 times. In 7 of the 26 patients with linitis plastica carcinoma, no metastases were encountered, while 8 patients of the control group were free from metastases.

Of the 7 patients without metastases, 4 were operated upon, but the tumor was found to be inoperable. Yet at autopsy no metastasis was encountered. Two of the other 7 patients were not subjected to surgery because their conditions were considered to be too weak. The 7th patient, 80 years old, was not operated upon because of her age. Among the 8 patients of the control group who were found to be free from metastases, 4 were operated upon and a partial gastrectomy was performed. A 5th was found to have an inoperable tumor. In 2 other patients of these 8 the gastric carcinoma had not been diagnosed clinically, and in the last instance, the patient was too anemic to be subjected to operation. In short, among 9 patients with gastric carcinoma and no metastases who were subjected to operation, all with linitis plastica type of carcinoma on exploration were declared inoperable (4 instances) as compared with only 1 patient of the miscellaneous cancer group (5 instances). Thus, it is evident that in some cases the linitis plastica type of carcinoma must have been present for a considerable time, and that extensive involvement of the stom-

plastica type had metastases to the peritoneum, peritoneal and retroperitoneal lymph nodes, liver, pancreas, colon, diaphragm, lungs, and pleurae.

#### EVALUATION OF STUDY

The gross and microscopic studies of these cases left no doubt that the principal lesion in the stomach, in every instance, was a diffusely infiltrating carcinoma, with marked subacute and chronic inflammation and subsequent diffuse fibrosis. It is clear that grossly and in a number of microscopic sections this lesion corresponded closely to the lesion named *linitis plastica*. However it must be remembered that—as Ewing pointed out—Brinton, who coined the term "*linitis plastica*" was by no means certain that the process was not cancerous. Ever since Brinton, and even before him (see Howard for an extensive review of the literature) the question was often raised as to whether *linitis plastica* was an inflammatory lesion or a tumorous one. This controversy became quite apparent as late as 1917 when the various views were aired at the meeting of the German Pathological Society. More recently an inflammatory origin of *linitis plastica* was strongly emphasized by Oselladore who claimed also that he was able to produce in dogs experimental lesions indistinguishable from *linitis plastica* in the sense of inflammation, by injection of diluted silver nitrate solution into the stomach. Saltykow also more recently described instances of contracted stomach as the result of healed phlegmonous inflammation, and Surran stressed that nothing suggestive of carcinoma could be found in the patient observed by him.

From the foregoing information it is evident that there are recently recorded instances of inflammatory lesions of *linitis plastica* type. Yet, combing the records of autopsy and surgical material, comprising 6520 autopsies, we did not find a single instance of *linitis plastica* of the inflammatory type or a contracted stomach in which, sometimes only after extensive search, tumor cells were not demonstrable. There are of course, instances of disease in infants diagnosed clinically as pyloric stenosis which at autopsy showed hypertrophy of the pyloric muscle without any evidence of tumor. But neither grossly nor histologically can these instances be confused with *linitis plastica*. Among the autopsies mentioned there was a single case which was interpreted as syphilis of the stomach. However the lesions were not diffuse, but localized in the fundic region and close to the cardiac end. There were typical scars and large accumulations of lymph-

ocytes around smaller arteries which showed endarteritic changes. Besides, there were scars in the left lobe of the liver to one of which the stomach was adherent. Neither grossly nor histologically could these lesions be confused with a *linitis plastica* type of carcinoma. The characteristic of syphilis in the stomach has been stressed previously by Fabr.

Dark cells without recognizable cytoplasmic hyperchromatic, irregular nuclei are of frequent occurrence since they resemble inflammatory cells and constitute, in many sections, the only structural cells. From a review of reported cases of *linitis plastica* of both the cancer and the inflammatory type it is evident that these cells have often been encountered. We stressed the findings of occasional collections of darkly stained cells which were diagnosed as "probably tumor cells. Ewing who believed that *linitis plastica* is a peculiar form of gastric carcinoma—the sclerotic, pykic, and diffuse fibrocarcinoma—emphasized that in regard of the fact that epithelial cells in this type of cancer may be reduced to a minimum or may largely disappear, had led to belief in the existence of supposed benign climosis of the pyloric region of the entire stomach. On microscopic examination Ewing found cells with hyperchromatic nuclei, and isolated cells with mucous globules as well as single rows of cells resembling plasma cells in the fibrous tissue. He concluded that all cases of hypertrophic pyloric stenosis and diffuse fibrosis of the stomach in adults are atypical fibrocarcinoma. The results of our study are in agreement with Ewing.

**Histological findings.** The histological findings in these cancers warrant their classification as a special entity. Though "scirrhus" cancer is often used as a synonym for *linitis plastica* type of cancer. It must be emphasized that "scirrhus" simply implies the firm consistency of the tumor. "Scirrhus carcinoma," by definition, is more likely to be a carcinoma simplex with cords and bands of cells, rich in collagenous tissue. There can be no question that such a scirrhus carcinoma exists in the stomach, but from the foregoing material it is clear that the *linitis plastica* type of carcinoma is strictly a different entity.

From the histological study it is apparent that this carcinoma is originally an adenocarcinoma, with the production of mucin by some of the individual cells. As has been pointed out by one of us (19) in a study of mucinous carcinoma of the mammary gland, there are a principal type of mucinous adenocarcinoma, one—the true mucinous carcinoma, in which the mucinous material

patients with gastric carcinoma and no metastases who were subjected to operation, all with the linitis plastica type of carcinoma on exploration were inoperable (4 instances) as compared to only 1 patient of the miscellaneous group (5 cases). Grossly, and particularly histologically, the linitis plastica type of carcinoma must be differentiated from other types of carcinoma. It is characterized histologically by subacute and chronic inflammation with much fibrosis and hyalinization, by the presence of small darkly stained cells with little cytoplasm, of small cells of low cuboidal shape with transitions to typical signet ring-shaped cells, and by miniature glandular structures. Metastasis in the liver was found only 1 time, whereas among the 40 miscellaneous types of carcinoma of the stomach the liver was involved 19 times. Among 6 females, the ovaries showed metastases 3 times, whereas among 6 males of the miscellaneous group the ovaries were involved only once.

It is very questionable whether linitis plastica, in the sense of a purely inflammatory lesion, exists. Among 6,520 autopsies there was not a single instance observed. The only chronic inflammatory lesion in the stomach, in this group, was diagnosed as the result of syphilis. The chronic inflammatory changes in the stomach in instances of the linitis plastica type of carcinoma with severe fibrosis may be explained on the basis of early, so called, serous inflammation and resulting overgrowth of connective tissue as it is known to occur in other organs.

## REFERENCES

- 1 BRINTON, W. Lectures on Diseases of the Stomach 2d ed. Philadelphia Lea & Blanchard, 1865
- 2 CHIRAY, M., and ALBOT, G. Arch. mal. app. digest., Par., 1935, 25, 841
- 3 DIXON, C. F., and STEVENS, G. A. Ann. Surg., 1936, 103, 263
- 4 EPPINGER, H., KAUNITZ, H., and POPPER, H. Die seröse Entzündung. Eine Permeabilitäts-Pathologie. Berlin J. Springer, 1935
- 5 EWING, J. Neoplastic Diseases, A Treatise on Tumors 4th ed. Philadelphia and London W. B. Saunders Co., 1940
- 6 FAHR, T. In the discussion of Henkes, F.'s report. Verh. Deut. path. Ges., 1927, 22, 93
- 7 GORMSEN, A. H. Ugeskr. læger, 1938, 100, 886
- 8 HOWARD, C. P. Q. J. Med., Oxf., 1933, 59, 26
- 9 JØRGENSEN, J. V. Acta path. microb. scand., 1935, 12, 193
- 10 JUDD, J. R., LARSEN, N. P., and TILDEN, I. L. Surgery, 1939, 6, 278
- 11 KROMPECHER, E. Beitr. path. Anat., 1910, 49, 384
- 12 LYLE, H. M. Ann. Surg., 1911, 54, 625
- 13 MONSERRAT, C. J. Philippine Islands M. Ass., 1940, 20, 75
- 14 OSELLADORE, G. Sulla patogenesi della linitis plastica dello stomaco. Contributo clinico e sperimentale. Arch. ital. mal. app. diger., 1937, 6, 295
- 15 PREMOLI, J. A. Contribución a su estudio clínico-anatómico patológico. Rev. méd. Rosario, 1940, 30, 351
- 16 RIVEROS, M. Linitis plastica. Tr. Cáted. semol. quiv. Asunción, Buenos Aires, 1941
- 17 RÖSSLE, R. Verh. Deut. Ges., 1934, 27, 152
- 18 SALTYSKOW, S. Beitr. path. Anat., 1935, 95, 450
- 19 SAPHIR, O. Surg. Gyn. Obst., 1941, 72, 908
- 20 SURREN, E. Chirurg. 1939, 11, 842
- 21 SURY, K., von Arch. VerdauungsLr., 1907, 13, 1
- 22 SUSSMAN, M. L. Am. J. Roentg., 1935, 33, 205
- 23 VIER, H. J. Rev. Gastroenter., 1938, 5, 319

ach renders the tumor inoperable yet no metastasis is found at autopsy.

The 2 patients, 1 male and 1 female with linitis plastica type of carcinoma of the rectum showed no metastasis at autopsy. There was nothing unusual in their clinical course. In 1 instance the diagnosis was made from a biopsy specimen. The patient with the carcinoma in the descending colon showed metastases to the ovaries, omentum, and peritoneal lymph nodes. As stated previously the patient with this type of primary carcinoma in the gall bladder showed diffuse metastases.

It is noteworthy that in 5 of these 16 patients, metastases were found in the intestinal tract. They were present in the transverse colon in 4 instances and in the descending colon in 1. They were recognized as metastatic lesions because they were smaller than the primary lesion in the stomach, and they had involved the peritoneal surface principally though the muscularis and submucosa were also involved. In 2 instances the mucosa was also invaded by the tumor. Besides the involvement of the omentum and adhesions of the latter to the stomach indicated the primary site in this organ. However in 1 instance the colon was the only site of metastases. Such observations have been made previously. Judd, Larnen, and Tilden reported an instance of apparent metastatic carcinoma of the linitis plastica type. The stomach had been removed some time previously. Gormsen found constricting rectal metastasis in his patient, and Dixon and Stevens reported 6 instances of metastases in the intestinal tract. Strumman's report also should be mentioned here. These observations are important since at operation such lesions might be considered primary tumors.

As stated before, in addition to the presence of tumor cells and subacute and chronic inflammation, these tumors are characterized by much fibrous connective tissue with hyalinization. The latter is occasionally explained by the simultaneous presence of chronic passive hyperemia. As a matter of fact, chronic passive hyperemia alone has been considered a cause of so called linitis plastica (Sury). Today it is obvious that chronic passive hyperemia plays a rôle either in the production of linitis plastica type of carcinoma or in the causation of a supposedly non-specific cirrhosis of the stomach, since this condition is never encountered in instances of uncomplicated heart failure of long duration which show severe chronic passive hyperemia in all the organs. However it seems possible to link the fibrosis of the stomach in these instances with

end-stages of so called serous gastritis. Eppinger, Kaulitz, and Popper defined a condition of the tissues as serous inflammation produced by the presence of plasma outside the capillaries. In the acute stage, there are hardly any elements forming the inflammatory exudate but it is principally an edema-like, or serous, inflammation. The significance of the concept of serous inflammation lies in the fact that, as the exudate and the plasma outside the capillaries even stimulates a connective tissue overgrowth, instances of severe fibrosis or sclerosis of the organs have been attributed to serous inflammation (Röske). It may be of interest to note in this connection that as early as 1910 Krogg referred to a relationship between edema of serous in the stomach. In the linitis plastica type of carcinoma, with diffuse infiltration of tumor cells throughout the wall, a serous inflammation is likely to occur. It has also been observed that the darkly stained tumor cells, a number of lymphatics. Thus, it is possible to attribute the extensive fibrosis of the stomach in these patients to the presence of plasma outside the vessel wall and to diagnose the resulting fibrosis as a sequela to so called serous inflammation.

As far as nomenclature is concerned, it is evident that the "linitis plastica type of carcinoma" is cumbersome but that it has the advantage of usage. Besides, "linitis plastica" seems to describe the gross appearance of the lesion adequately. The term linitis plastica should be discarded since the existence of a purulent inflammatory lesion such as this term denotes is very questionable. If diffuse inflammation is caused by syphilis do exist — but not — they may be so designated. However by using "linitis plastica" as a descriptive term, adding the fact that the lesion is cancerous as — "linitis plastica type of carcinoma" — there seems to be no objection to this term.

#### SUMMARY

Twenty-six instances of linitis plastica type of carcinoma of the stomach, 3 of the large intestine and 1 of the gall bladder are reported. The interval between the onset of symptoms referable to gastric disorders and death in patients with linitis plastica type of carcinoma was unusually short as compared to that of a control group of patients with miscellaneous gastric carcinomas. Also the postoperative survival period of the 5 patients who were operated upon seemed very short. Among 11 such patients, the survival period was 11 days or less. Among 15

lure, now prefers total hysterectomy and states that, while occasionally the supracervical operation should be performed, it should be performed only under the following conditions first, when there is a normal cervix, second, when there is a need for rapid conservative surgery as, for instance, when the patient is an especially poor operative risk. He makes the point that cauterization or conization of the remaining stump, following supravaginal hysterectomy, is of little or no value as compared with complete removal.

Most surgeons accept the proposition that neither the total nor the subtotal operation should be recommended as a *routine* procedure. Frequently, an occasion arises when one or the other, especially the less extensive, is clearly indicated, for example, when the patient is an extremely poor risk and the lesion benign. It seems clear that the total operation would be generally preferred were it not that it takes longer to perform, that it requires greater skill, and that, as is revealed from accumulated figures from unselected clinics, it is accompanied by higher morbidity and mortality.

In the most recent contribution on the subject from the Mayo Clinic, McKinnon and Counsellor report an experience with 1920 total hysterectomies performed in the 5 year period between 1935 and 1939. It is the belief of these writers "that every patient presenting a diseased cervix in association with other uterine conditions requiring hysterectomy, should have a *total* hysterectomy." They stress the advantage of eliminating the cervical stump which may become chronically infected or, ultimately, involved in carcinoma, and they point out that following this operation there is much better vaginal support than with the supravaginal type of procedure. Among possible complications they mention postoperative hemorrhage as occurring in 8 of their cases. They admit that pulmonary embolism is more common than is the case following subtotal hysterectomy, yet the incidence of thrombophlebitis seemed higher after subtotal than after total hysterectomy. On the other hand, they found the incidence of urinary complications, following total, somewhat higher than following subtotal. The number of convalescent days was slightly greater with patients submitting to a total, while there was "about a half a day" extension of elevated temperature. The mortality rate was commendably low, being 0.78 per cent for their total hysterectomies as against 1.4 per cent for the subtotal operations. These authors point out that, when a fatality ensues, peritonitis still remains the chief cause of death. Thirteen of the 23 hospital deaths were due to this complication, while 4 were trace-

able to pulmonary embolism and 2 to bronchopneumonia. In the presence of pelvic infection, they point out that mortality is definitely higher following total hysterectomy than following subtotal; hence, with this group, the operation of choice should be subtotal hysterectomy. Their conclusions are that the advantages of removal of the cervix far outweigh any known complication that may arise following total hysterectomy and, that except in cases in which there is known pelvic infection, total hysterectomy should always be the operation of choice.

In Masson's (6) latest contribution he expresses himself as more convinced than ever concerning the utility of the total operation and he again emphasizes that "the end-results are better, the morbidity less, and the mortality no greater than when a subtotal abdominal hysterectomy is done." Furthermore, he makes the statement, the truth which most of us will accept, that "for the occasional operator, or for one who has not yet taken special pains to become familiar with the technique of total abdominal hysterectomy, it is better to adhere to the subtotal operation, even the risk of leaving an infected cervix."

Masson refutes the claim that total abdominal operation is a frequent cause of dyspareunia. When such a condition is found, it is not the result, he states, of the operation as much as it is of the fact that the operation has been improperly performed. Fixation of the ovaries in the vault of the vagina is, he suggests, a common cause of this complication. Masson (6) reports that of a group of 1776 cases in which the total procedure was carried out at the Mayo Clinic, the mortality was 1.2 per cent. In a later series he reports a mortality as low as 0.76 per cent. Masson invariably removes the tubes in all hysterectomies. When the ovary is saved, he prefers to bury it between the folds of the broad ligaments well up on the side of the pelvis rather than to fix it in vault of vagina.

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Since Chrobak of Vienna reported the first case of carcinoma in the cervical stump in 1896, 169 cases had been recorded in Germany up to 1925. As early as 1921 Polak was able to collect 256 cases from the American literature alone.

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## TOTAL ABDOMINAL HYSTERECTOMY

HAROLD L. FOSS, M.D., F.A.C.S. and J. REED BABCOCK, M.D. Danville, Pennsylvania

THE operation of *complete* hysterectomy is being performed with increasing frequency in the treatment of lesions involving the uterus. With many surgeons practically all hysterectomies are of the total variety. Many arguments in favor of the procedure have been advanced, some have been raised in opposition. However, all phases of the question considered, a carefully planned technique and the operation performed by a skilled surgeon, the mortality and morbidity of total hysterectomy are no greater than those in subtotal hysterectomy and the results which are obtained, in many respects, are better.

Many methods for total removal of the uterus have been described. In our own country, Mason (6), Farrar (4) and Richardson (13) have described excellent procedures. During the past few years the senior author has attempted to better his own technique and believes that he has succeeded in simplifying and improving the operation. He has been aided by several instruments of his own designing and now feels that the operation has been sufficiently perfected to warrant its presentation. Of a total of 966 hysterectomies the senior writer has performed, this technique has been followed in 156 consecutive cases. During the past 18 months practically all of our hysterectomies have been carried out by this method. Only in cases of extremely stout patients or when, for some reason, the operation presents unusual technical difficulties or it is felt that the individual might be endangered by having the cervix removed, is it carried out routinely, whether the process be benign or malignant.

It is not the purpose of this paper to present extensively the arguments for or against total hysterectomy. Innumerable articles have appeared dealing with the problem, 98 contributions on the subject having been incorporated in our American literature within the past 8 years. The consensus seems to be that total hysterectomy possesses definite advantages over the subtotal operation and that, in competent hands, it is attended by as low mortality and morbidity rates as the supravaginal operation. This thesis, well supported by extensive statistical analyses, has been presented many times. It is endorsed by the present writers.

From the Department of Surgery, Geisinger Memorial Hospital.

### THE CERVIX AS A MENACE

The main advantage of the total operation is that the cervix, the site of infection or, possibly, neoplasm, is removed. It is the chief and, probably, the only point in its favor. The question arises as to whether or not the advantage of eliminating the cervix outweighs the disadvantages of slightly increased mortality and morbidity. Clearly, the complete operation requires more skill. In clinics where the work is handled by experts there is apparently no appreciable difference in mortality or morbidity. What this difference is in the innumerable small hospitals, where a sum total, most hysterectomies are probably performed, one cannot say.

It is clear, however, that if one advocates the complete operation, one must first be certain that the retained cervix is a definite hazard. To what degree this is true. Even now, however, one must be sure one possesses the necessary skill for the safe and proper performance of the formidable operation.

### PROS AND CONS

Richardson (13), comparing total with subtotal hysterectomies, offers certain arguments in favor of the complete procedure. He states that the incidence of cervical stump carcinoma at Johns Hopkins, among 940 patients having cervical carcinoma, was 2.3 per cent. He stresses the presence of infection in the retained cervix and notes that, with the proper technique, the difference in mortality between the two operations might as to be negligible. He concludes, "Consequently, despite its many alleged advantages, conservative subtotal hysterectomy has not only a limited field of applications." After considering the possible disadvantages of the complete operation, Richardson states that it may be accompanied by a higher incidence of postoperative hemorrhage, shock, and damage to the bladder, ureters, and rectum, with subsequent fistula formation, cystitis, pelvic cellulitis, wound infection, phlebitis, and thrombosis. He indicates, however, that these are no more common in the total operation, if it is expertly performed. He emphasizes the fact that the operation is one requiring great experience and surgical ability than is called for in the supracervical operation. Richardson, who formerly favored the more conservative procedure,

ure, now prefers total hysterectomy and states that, while occasionally the supracervical operation should be performed, it should be performed only under the following conditions first, when there is a normal cervix, second, when there is a need for rapid conservative surgery as, for instance, when the patient is in especially poor operative risk. He makes the point that cauterization or conization of the remaining stump, following supravaginal hysterectomy, is of little or no value as compared with complete removal.

Most surgeons accept the proposition that neither the total nor the subtotal operation should be recommended as a routine procedure. Frequently, an occasion arises when one or the other, especially the less extensive, is clearly indicated, for example when the patient is an extremely poor risk and the lesion benign. It seems clear that the total operation would be generally preferred were it not that it takes longer to perform, that it requires greater skill, and that, as is revealed from accumulated figures from unselected clinics, it is accompanied by higher morbidity and mortality.

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At the Mayo Clinic, among 1181 cases of carcinoma of the cervix observed over a short period of time, there were 47 cases or 3.97 per cent, of carcinoma of the cervical stump. The following is an illustration of the gravity of late development of carcinoma in retained cervixes. Of 65 patients who were treated for carcinoma of the cervical stump at the Mayo Clinic and whom he was able to trace thereafter Masson (6) found but 30 per cent living at the end of 5 years. From January 1910, to January 1937 the Mayo Clinic had 146 cases of carcinoma of the cervix following subtotal hysterectomies.

Masson disagrees with those who feel that the cervix can be adequately treated, either before or after a subtotal hysterectomy by various procedures such as, trachelorrhaphy, cauterization, or low amputation. Von Guelf reports 37 cases of carcinoma developing in cervical stumps following partial hysterectomy even after the cervix had been cauterized, or coned out, at the time of the hysterectomy.

Farrar (5) points out that all recent reports give increasingly larger percentages of cancers developing in the stumps of cervixes left after subtotal hysterectomy. All persons interested in this subject should become familiar with the paper by this author, in which she presents a painstaking study of conditions existing in the cervix following 570 consecutive total abdominal hysterectomies. As set forth in this communication, it is reasonable to believe "that a growth hormone that has effectually stimulated the development of myomas in the corpus, may also cause profound changes in the cervix and that after the removal of the corpus by subtotal hysterectomy the same hormones may continue to produce alterations in the cervix which eventually may be favorable to the development of cancer. Farrar notes that at the Women's Hospital in New York seven to eight per cent of all cases of cancer of the cervix occurred in cervical stumps. The most significant conclusion arrived at in Farrar's paper is worth quoting in full:

Carcinoma of both corpus and cervix uteri is more frequent in myomatous uteri. The repeated occurrence of glandular hyperplasia and cystic degeneration in the cervix when myomas are present in the body of the uterus would seem to point to a common stimulus affecting the tissues in both corpus and cervix and make it advisable to remove the uterus as a whole rather than leave the lower portion in situ subject to still further stimulation and the danger of infection, local or systemic, the formation of polyp or cervical myoma and the possibility of carcinoma developing in the stump.

In a discussion of the subject Scott states that in a series of 49 cases of cancer of the cervix ob-

served at the Toronto General Hospital, 175 were 20 in which cancer had formed in cervix cervic.

Masson (6) tells us that, at the Mayo Clinic while they reported 164 cases of carcinoma originating in cervical stumps, they had also treated 500 other patients who were supposed to have cancer in the cervix, following a previous cone, vaginal hysterectomy; yet in all these cases a benign condition was found. However, with about one-half of these patients extensive infection or infective processes necessitated excision of the cervix.

#### MORBIDITY AND MORTALITY OF TOTAL HYSTERECTOMY

Bryan and Trabue, in a study covering 200 operations performed by a large number of surgeons, found a mortality of 1.73 per cent in 216 subtotal operations compared with a mortality of 3.38 per cent in 8,443 total hysterectomies.

Tyrone, reporting from a smaller series, gave a mortality of 1.9 per cent for 316 subtotal hysterectomies as against 2.3 per cent for 137 total operations. The author stated that the difference in time required for these different procedures is slight, not averaging over five minutes.

McDonald strongly advocates total hysterectomy as a routine procedure in benign as well as malignant conditions of the uterus. In one hospital he reports 2628 consecutive total operations performed by 10 surgeons, with a mortality of 1.02 per cent. He observes that the operation requires but a little more time than the subtotal procedure to support his findings he quotes Fisher whose studies in anesthesia time show that but 15 minutes more are required, and he also cites Goodall who gives the additional time as 5 "more more than fifteen minutes.

In 1937 Masson (7) presented a large series of hysterectomies performed at the Mayo Clinic together with an analysis of the questions of morbidity and mortality and length of hospital stay. Included in the report were 95 total abdominal hysterectomies showing an average period of hospital convalescence of 16.5 days and a 1.4 per cent mortality. There were 451 subtotal hysterectomies with an average hospital stay of 16.2 days and a .3 per cent mortality. There were 23 vaginal hysterectomies with 18.4 hospital days and a 1.9 per cent mortality. The figures are revealing and coming from a well equipped clinic where the operations have been performed by men of great skill, clearly demonstrate that in capable hands, there is only a negligible difference between the mortality and morbidity rates in all three

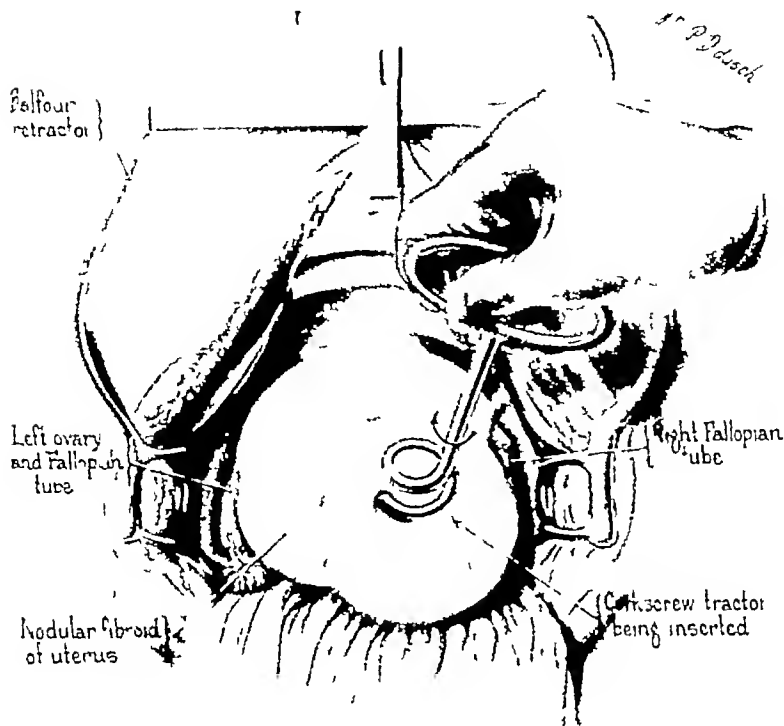


Fig. 1 Through a vertical midline incision between the pubis and umbilicus a Balfour retractor is inserted and the tumor raised into the wound by any suitable means. A corkscrew type of retractor is helpful with myomatous types of neoplasms.

types of procedures utilized in the removal of the uterus.

One of the most informative studies made of the question of mortality and morbidity rates is that of Read and Bell. In this investigation over 2,000 consecutive operations performed at the Chelsea Hospital for Women by 14 English surgeons are analyzed. In 1,700, or 70 per cent, supravaginal operations were performed while in 605, or 25 per cent, total abdominal hysterectomies were done. Under the heading of "morbidity" the authors include all patients whose stay in the hospital, following the operation, exceeded 21 days. From the study it was found that the "morbidity" rate was 20 per cent for the subtotal group, with a mortality of 2.1 per cent, while for the total hysterectomy group, "morbidity" was 27 per cent and mortality 3.1 per cent. An examination of these statistics demonstrates that, at least in the cases of these patients, operated upon by a number of surgeons, convalescence was more prolonged following the total than it was after the subtotal operations, while the mortality rate was higher by about 1 per cent. Abdominal wall rupture occurred twice

as frequently after the total operation as it did after the subtotal procedure.

Many authorities claim that dyspareunia is a frequent complication following total hysterectomy. However, others believe that it rarely, if ever, occurs provided the operation is properly performed. The latter attitude is taken by Mason, Haney, and many others.

In discussing the possible dangers of total hysterectomy, Eddy and Miller reviewed the cystoscopic findings of 200 patients on whom total hysterectomies had been performed. Of this group, 1 patient had a ureteral stricture, 3 had angulated ureters, and 15 had atonic bladders; in addition, there were 13 cases of plevitis and 35 of cystitis.

Farrar (5), in speaking of the greater technical difficulties of total hysterectomy, makes the following statement: "I have never minimized the fact that a total abdominal hysterectomy is more of an operation to perform than a subtotal, but I do maintain that it is often the better operation for the patient. It seems to me major surgery would never have reached its present height if its

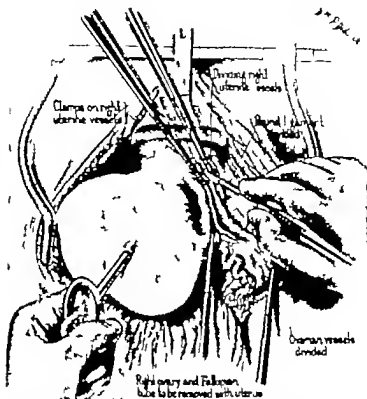


Fig. One or both ovaries are preserved or removed depending on type of tumor, the patient's age, and other factors, this step of the technique varying with individual conditions. The uterine vessels are clamped and divided, the round ligaments are divided and ligated and, in case of removal of the ovaries, the ovarian vessels are secured.

standards had been kept on the level of the *least ad rem*. A terse, significant, and accurate statement. However this author points out that, in 50 consecutive total abdominal hysterectomies performed by 37 surgeons in a hospital devoted strictly to diseases of women, the total operation had the greater morbidity rate. It might be concluded that not all those who operated were experts.

In the Farrar series there were 406 total hysterectomies for benign conditions, with a mortality of .9 per cent. In the same institution in a series of 300 operations performed prior to 1938, the mortality for supra vaginal hysterectomy was per cent. It was shown that more than half the deaths were due to infection, an obviously preventable condition, and, therefore, it was emphasized that one of the most important things to consider in mortality reduction is more thorough preoperative preparation of the vagina.

#### THE OPERATION

The senior author believes that it would be appropriate to describe an operation of lesser devising which, perhaps, is no more than a elaboration of procedures suggested by others. It employs certain instruments, in particular a vaginal clamp which simplifies the operation, requiring no more difficult nor time consuming than the operation in which the cervix is permitted to remain. In the author's experience it has been marked by satisfaction in low mortality and morbidity rates. The mortality for 70 consecutive patients operated upon by this method was .14 per cent. The average period of hospital stay for the last 50 consecutive patients, was 13.5 days, 5 per cent of the patients returning to their homes within 1 day or less. The patients in the series died. In both instances a topology was performed. It was found that 1 patient had an intestinal obstruction due to adhesions from a previous operation.

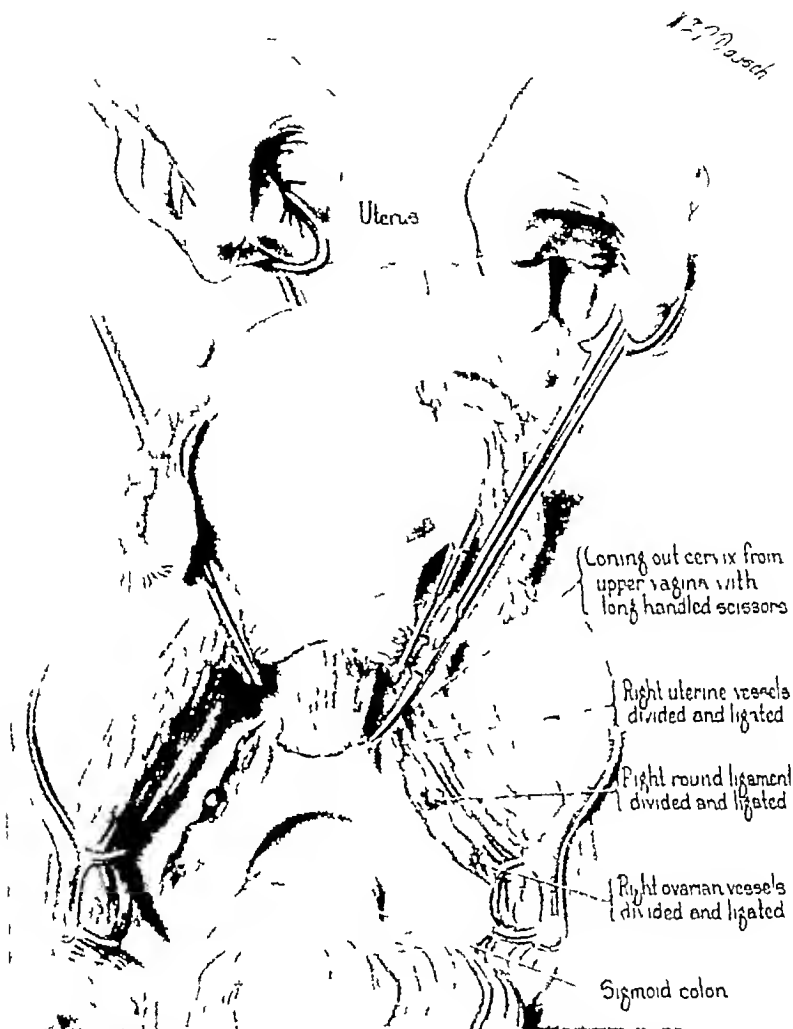


Fig 3 After the isolation and division of both uterine arteries, the uterus and cervix are carefully dissected free from the surrounding cellular structures, great care being taken to remain close to the cervix so as to avoid damage of the ureters

tion while the other died from pelvic sepsis, due possibly to incomplete vaginal preoperative preparation, obviously an avoidable condition. The 156 total hysterectomies performed by this technique were carried out for the relief of the following conditions: fibroids, 112, carcinoma of fundus or cervix, 14, endometriosis, 9, carcinoma of ovary, 3, in conjunction with removal of ovarian cysts, 9, in addition to abdominoperineal resection for carcinoma of rectum, 1, miscellaneous pathological processes, 8.

**Technique**—The patient should have a cleansing douche administered the evening before the

operation followed by the introduction of a vaginal antiseptic that is germicidal, but not irritating. The following morning, after the anesthetic has been administered, and our preference is for spinal almost routinely, the patient is placed in the lithotomy position, and the vagina again is thoroughly cleansed. The solution used is one which we apply in abdominal skin preparations. It was developed at the University of Minnesota by Novak. It is nonirritating, is powerfully germicidal, and has proved a most satisfactory medium. The formula for the cleansing solution is given as follows:

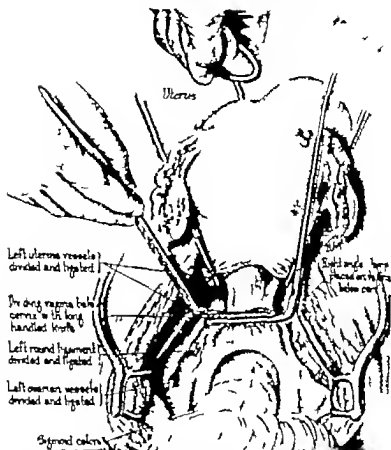


Fig. 4. With bleeding from the uterine and cervical vessels controlled, the bladder is pushed well away from the dome of the vagina, it being replaced anteriorly by means of a bladder retractor. A special right angle clamp is then placed across the upper portion of the vagina, immediately below the cervix, and firmly locked. The upper vagina is then divided, just above the clamp, with one sweep of the right angle knife.

#### Chemical Solution Formulae

Alcohol (95%)	550 c.c.	Tricresol (Lyons)	5
Acetone	100 c.c.	Mercuric chloride	7 grs
Water	375	Eosin Y	6 grs
		Acid fuchsin	66 grs

The patient is placed in the Trendelenburg position, and the usual vertical incision between the umbilicus and the pubis is made, which in case of a large tumor is carried to the left and above the umbilicus. After the peritoneum has been opened and the wound is protected with towels, a Balfour retractor is inserted and the intestines are gently packed off in the upper abdomen. Traction is then placed either upon the fundus or on the tumor itself. When the tumor is myoma, a corkscrew type of retractor will be found particularly helpful. The ovaries are preserved, or removed, according

to the indications, the patient's age, and the type of tumor. If the ovaries are to be excised, the broad ligaments are clamped and the ovarian vessels are secured and ligated. The peritoneal reflection covering the bladder and the anterior surface of the uterus is carefully divided, and the bladder is pushed well downward and anteriorly. This step is extremely important. The bladder should be thoroughly separated from the anterior surface of the cervix and the upper vagina, otherwise, in the later stages of the operation, there is possibility of its being injured by the needle with the right angle clamp to be described later. In carefully dissecting the bladder from the anterior surface of the cervix and holding it well forward by means of a retractor, damage to it can be completely avoided.

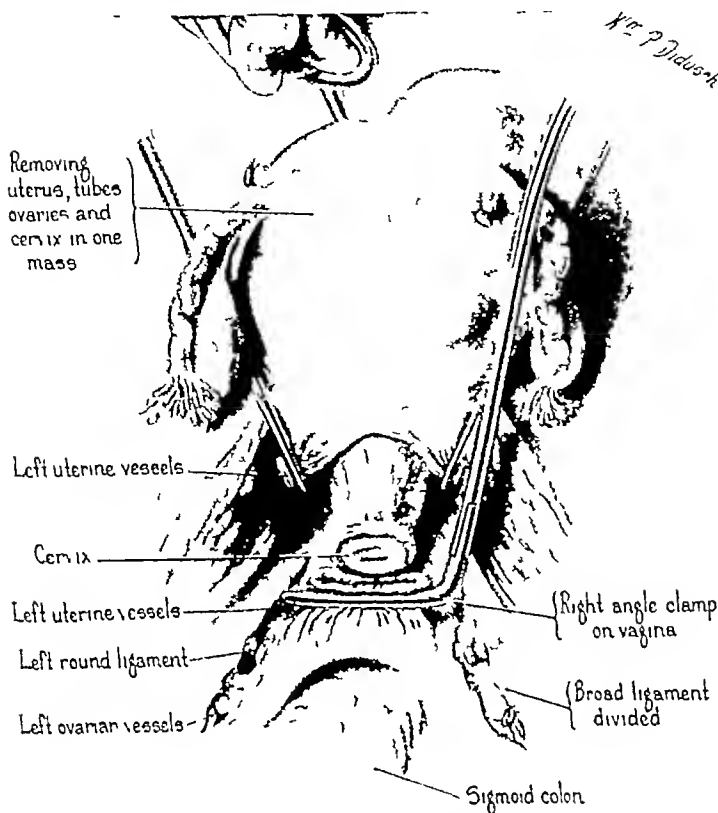


Fig 5 The uterus with tubes and ovaries, provided they are to be removed, is then removed from the pelvis. Contamination from the vagina and bleeding from its divided surfaces are completely controlled by the clamp.

The incision is now carried down until the uterine vessels are exposed, at which stage they are clamped, divided in the usual manner, and secured by a transfixion suture. Meanwhile, the round ligaments have been divided close to the uterus and ligated. The stumps of the uterine arteries are then gently pushed downward by means of gauze sponges after which branches of the cervical arteries are secured and tied. The positions of the ureters are definitely determined and constantly borne in mind. While firm, upward traction is maintained on the uterus, the cellular tissue overlying the cervix is divided, the dissection being kept close to the cervix at all times so as to avoid the ureters. Continuing the operation, the dome of the vagina is separated, anteriorly, from the cellular structures between it and the bladder as well as laterally and posteriorly, in the same manner. Areolar tissue attached to the cervix should be gently pushed down by means of a piece of gauze held in a pair of long finger dressing

forceps. One must be sure that the ureters are well out of the way before application of the transverse vaginal clamp which is then applied across the upper portion of the vagina, immediately beneath the cervix, and locked firmly in position. By means of the angle knife the vagina is cut across immediately below the cervix and above the jaws of the clamp. The clamp completely prevents contamination from the vagina and effectively controls bleeding from the cut margins of the vaginal walls. The tumor is then removed in one mass together with the uterus and the cervix. The vaginal dome is next closed by means of a running mattress suture of chromic catgut placed back and forth beneath the clamp in an antero-posterior direction, then the clamp is removed, the suture being continued back across the vaginal cuff so as to pick up the severed margins of the mucous membrane in an over and over running suture. At this stage, it has been our custom, before implanting the round ligaments, to sprinkle



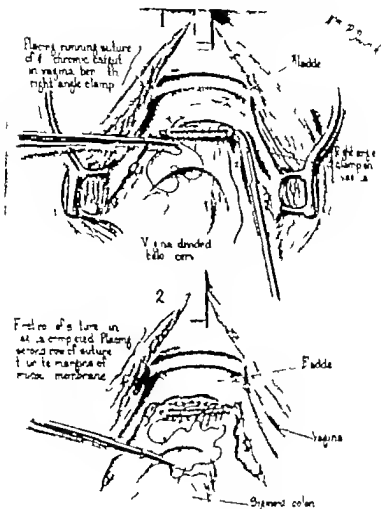


Fig. 6 The vagina is then closed by means of a running continuous, mattress suture of chromic catgut placed beneath the clamps. The clamp is then removed and the suture continued back as a continuous, overlapping one placed in the vaginal margins. In excellent practice, at this step, is to sprinkle 1/2 gram of sulfanilamide over the exposed surfaces before peritonealization is carried out.

one-half gram of crystalline sulfanilamide over the stump of the vagina and surrounding raw surfaces.

The ligaments are then approximated. Frequently if sufficiently long they are overlapped and firmly sutured to the dome of the vagina by means of interrupted sutures of catgut so as to produce an effective support. The whole area is then thoroughly peritonealized by means of continuous suture passing from one round ligament to the other and laterally from the dome of the vagina to the ligated ovarian arteries. Small

the lateral sutures are placed intermittently for if a continuous suture is used, there is danger of kinking and possibly of blocking the cervix (Fig. 7).

With most total operations, at the time of the removal of the cervix, the vaginal canal is widely exposed. Such a condition presents no special danger if the vagina has been carefully prepared. It is unusual, even momentarily, to see the canal of the peritoneum with highly keratinized mucous membrane which might infect it.

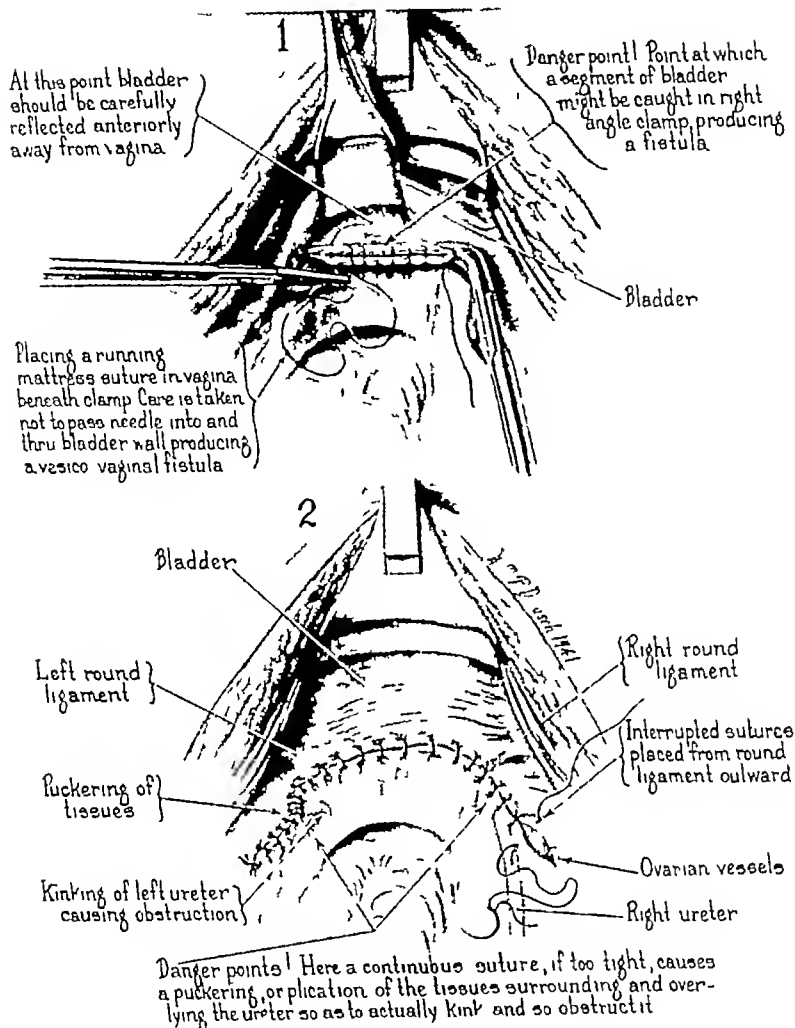


Fig 7 This illustration was especially prepared to emphasize two possible danger points in the operation. The upper figure illustrates the means by which the bladder is retracted forward. If this detail is not carefully observed a suture may pass through the bladder wall or, a part of the bladder may be caught in the clamp producing a vesicovaginal fistula. In the lower figure the importance of avoiding kinking the ureter is stressed and method of its prevention illustrated.

only the peritoneum but also the highly susceptible extraperitoneal tissue spaces which are necessarily exposed during the operation. In seeking an improvement in technique, it was evident that a desirable feature would be some device for firmly clamping the vagina and holding the margins of the severed mucous membrane in a closed position during suturing. The clamp effects this perfectly. The design of the jaws follows that of the smaller of the three Payr clamps used in stomach resections. Besides the usual pin found in the Payr

clamp, a second pin, near the turn of the jaws, is provided, which effectively prevents the vaginal cuff from slipping laterally. The clamp is of rugged construction and is 9 inches long so that it will reach well outside the abdomen. The handles, flexed slightly to facilitate application of the instrument in the hands of the first assistant, are provided with a heavily constructed lock designed to secure the vaginal margins tightly.

A pair of long, curved, heavily constructed, Mayo dissecting scissors, facilitates dissection of

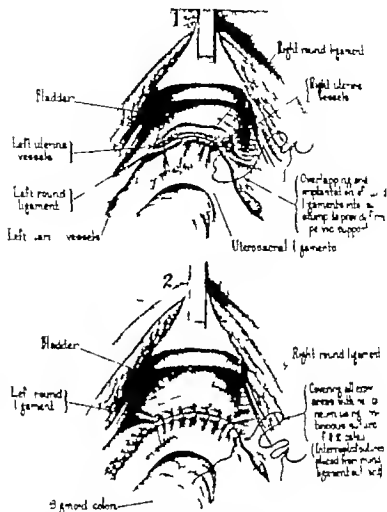


Fig. 8. Further steps in the operation are represented in this drawing, which shows the means by which the round ligaments are sutured into the dome of the vagina to provide support. As a general thing, the round ligaments are approximated, or even overlapped, thus providing more support than is indicated in the illustration. The entire area is then completely peritonized.

the cervix. A long handled, angulated knife holder with the blade set at 30 degrees, constructed by Bard-Parker from the senior author's design, completes the set of required instruments. From time to time it is our custom to have the points of a dozen or so No. 10 Parker blades rounded off on a wheel. A stock of these blades is always kept on hand. Rounding the point prevents damage to the bladder at the time of sectioning the vagina.

In the performance of every total hysterectomy two possible dangers must be borne in mind. If

they are forgotten, or if one becomes careless, the advantages of total hysterectomy may be completely offset by complications which may not only add to the patient's period of hospitalization but which may even result in a fatal termination. This operation, like other operations of a highly technical nature, must be skillfully performed. It should never be attempted with the carelessness with which the surgeon might approach a supravaginal removal, yet it is an operation which should cause him no greater anxiety if he

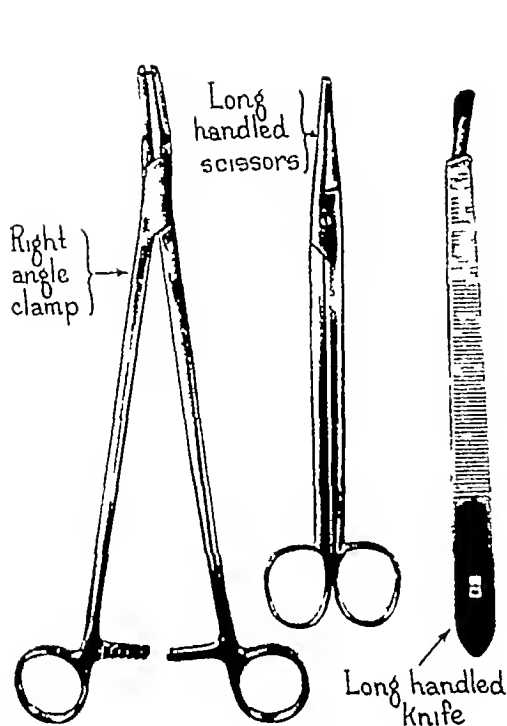


Fig 9

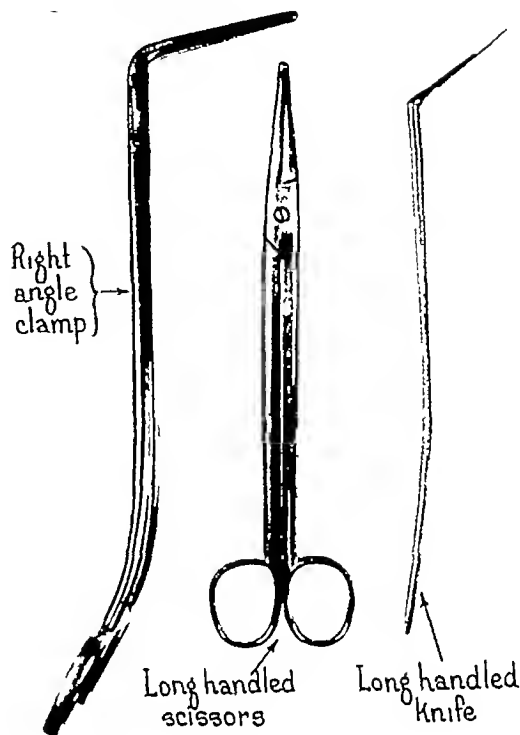


Fig 10

Fig 9 The instruments which greatly facilitate the operation are here illustrated. They consist of a A right angle clamp of especially rugged construction, in the jaws of which are two pins which effectively prevent the vaginal dome from slipping laterally b, A pair of long rugged Mayo dissecting scissors, the length of which is 9 inches c A right angle knife handle holding the usual No. 10 blade, the point of which has been rounded off on an emery wheel so as to avoid injury to the bladder

Fig 10 Lateral view of clamp and knife

Fig 11 The vaginal clamp

Fig 12 Close up of jaws of clamp

Fig 13 The right angle knife



Fig 11

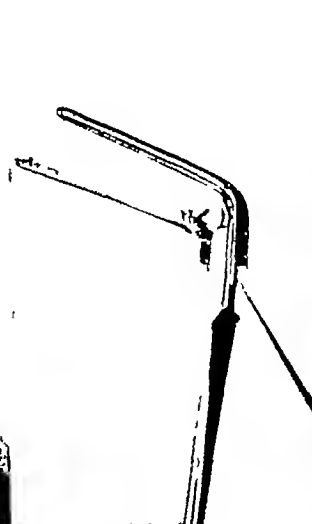


Fig 12



Fig 13

has the necessary skill, if he has mastered the anatomy of the pelvis, and if he proceeds with due caution, constantly bearing in mind certain dangers inherent in the procedure.

The first possible danger is injury to the ureter. There is no excuse for its occurrence if one bears in mind the position of the ureter or better if he has it under his eyes throughout the dissection. It may occur during the suturing of the broad ligaments and closure of the peritoneum laterally at which time the ureter may be inadvertently kinked. If the sutures are pulled too tightly, especially if a deep continuous suture is used, the ureter may be angulated sufficiently to obstruct it. This complication cannot occur however if one keeps the ureter in view or constantly bears in mind its position and particularly if one is careful to work close to the cervix during its dissection and excision.

The second danger is an inadvertent puncture of the bladder in the process of suturing the cuff of the vagina which usually results in a vesicovaginal fistula. Either of these two complications may develop without being detected until late in the patient's convalescence. How to avoid them is graphically described in one of the accompanying drawings (Fig. 7).

#### SUMMARY

No one is unmindful of the fact that if total hysterectomies were performed routinely by all surgeons, both those of great skill as well as by those of limited experience in pelvic surgery, mortality would be high. The imperfectly trained surgeon or the surgeon with little experience who let us say performs not more than 6 or 8 hysterectomies a year should confine himself to the supracervical procedure. It is probably true that if all hysterectomies were of the complete type the final mortality would be greater than it is now with supravaginal hysterectomies, plus cancer deaths, resulting from neoplastic disease developing in the retained cervix.

To advocate total hysterectomy to all surgeons throughout the country with all patients, to prevent the occurrence of carcinoma in the cervical stump, would cause far more deaths than would the carcinoma itself (Melfs).

In a recent discussion before a medical gathering it was mentioned that during the past 5 years in one hospital 280 hysterectomies had been performed by 10 operators. One surgeon stated that he was convinced the mortality and morbidity of panhysterectomy is too high price to pay for the possible advantages of the procedure. The average number of operations performed annually

by each surgeon in this hospital is 28. It is obvious that surgeons of limited experience should select the less formidable type of procedure.

When does a surgeon become an expert? How many years must he work before he can be pronounced thoroughly skilled? How many operations of a given type must he perform before he may be considered particularly destimé in the treatment of the condition for which this particular operation is performed? Given technically perfect procedure requiring great experience for its execution, how many times must the surgeon carry it out before he becomes fully experienced? Fifty or hundred or five hundred times before he can be accepted as thoroughly proficient in the procedure. Consider two surgeons of equal ability. Which of the two is likely to be the more successful—the one who performs the operation once 100 times each year or the one who does not until his first hundred until the end of his tenth year? In aviation, skill is graded largely by experience and experience is measured by the number of hours the pilot has flown. A pilot must have 100 hours of flying before he can obtain a private pilot's license. He must have 1,000 hours before he can secure a commercial license. Moreover the airlines will not accept him even as a pilot until he has had at least one thousand hours in the air.

Of course we cannot grade surgeons as we grade aviators yet it is logical to suppose that the surgeon who has performed a difficult procedure 100 times does not possess the skill of the man who has performed it one hundred times. So it is with hysterectomies. The surgeon who performs one or two hysterectomies a month should not attempt the supravaginal procedure. Such a man should consider himself broadly experienced. Finally, the ability the man who performs hundred times each year should be able to carry out the operation expertly with a mortality no greater than that of the surgeon who adheres to the less formidable procedure.

We agree with Mason with Richardson with all men there who have written on the subject that it does not necessarily mean that total abdominal hysterectomy is dangerous when performed by one experienced and proficient in pelvic surgery. It is not a procedure for the occasional operator. It is for the thoroughly trained and experienced surgeon. With him it is a safe procedure and the majority of patients requiring a hysterectomy total abdominal hysterectomy is, by all standards, the best procedure.

## REFERENCES

- BRYAN, WORCESTER, A, and TRABUE, CHARLES C  
Ann Surg, 1936 103 914-923
- CHROBAK, R. Mschr Geburtsh Gyn, 1896, 177
- EDDY, R W, and MILLER, F H Am J Obst, 1937,  
33 85-90
- FARRAR, LILLIAN, K P Surg Gyn Obst, 1935, 60  
827-839
- Idem Tr Am Gyn Soc (1939), 1940, 64 248-  
259
- MASSON, J C Am J Surg, 1940, 48 255-265
- Idem Surg Clin N America, 1937, 17 1131-1142
- 8 McDONALD, EDWARD P N York State J M, 1939,  
39 503-508
- 9 MCKINNON, D A, JR, and COUNSELLER, VIRGIL S  
Surg Gyn Obst, 1942 74 957-960
- 10 MEIGS, J V Am J Obst, 1936, 31 358-366
- 11 POLAK, JOHN OSBORNE J Am M Ass, 1920, 75 579
- 12 READ, C D, and BELL, A C J Obst Brit Empire,  
1933, 40 749-767
- 13 RICHARDSON, E H Am J Obst, 1935, 30 237-243
- 14 Idem Surg Gyn Obst, 1929, 48 248-256
- 15 SCOTT Discussion of Farrar's paper (5)
- 16 TYRONE, C H Ann Surg, 1938, 107 836-841
- 17 VON GRAFF, E Am J Obst, 1932, 23 195-199

## ACUTE SUPPURATIVE TENOSYNOVITIS OF THE HAND

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**S**UPPURATIVE tenosynovitis of the flexor tendons of the hand presents a problem which has not been solved surgically. This problem is of extreme importance physiologically, surgically, and economically. Acute infections of the flexor tendon sheaths of the hand are relatively common and are frequently followed by total or partial loss of the part involved.

Results in the present group of cases show no improvement over those reported 30 years ago. Despite this fact much progress has been made in our knowledge of the anatomy, bacteriology, pathology, and therapeutics of tenosynovitis of the hand. This present study supplies some facts concerning the natural history, reveals defects in past treatment, and provides some suggestions which, if followed, should improve our results.

## ANALYSIS OF STUDY

The material studied consisted of 100 cases of acute pyogenic infection of the flexor tendon sheaths of the hand, in which patients were treated at the Boston City Hospital. Most of the patients were followed for 20 months.

As to the origin of the infection, we found that it was either of (1) direct origin, in which case there was direct inoculation of the tendon sheath, or (2) indirect origin, in which case the infection spread from a neighboring pathological process. In this series 57 per cent were of direct origin and 43 per cent of indirect origin. In no case in the series did the infection spread via the blood stream—6 cases of gonococcus tenosynovitis, which are blood borne, are not included in this series. In no case did the infection spread via the

lymphatic system. Forssell reported cases of lymphatic origin and Kanavel also believed that such infection could be of lymphatic origin.

The cases were classified on the basis of functional result.

In group 1—the bad results—are included (1) sloughed tendons with loss of flexion of the middle phalanx or distal phalanx, or both, (2) ankylosed proximal or distal interphalangeal joint, giving a stiff finger—motion in the metacarpophalangeal joint may or may not be present, (3) amputations, and (4) deaths.

In group 2—the fair results—are included (1) partial function of tendons, the limitation usually being caused by adhesions, (2) active, but limited, motion in the proximal or distal interphalangeal joints, or both. There may be normal or slightly limited motion in the metacarpophalangeal joint, fist cannot be made actively, but adjoining fingers may be used in making extreme flexion.

In group 3—the optimum results—are included (1) normal or almost normal function of tendons, (2) complete or almost complete flexion of the distal and proximal interphalangeal joints. There may be slight limitation of extreme flexion. Function of the fingers is practically as good as before infection.

As to the cause of the infection, we found that puncture wounds are the most common type of injury causing septic tenosynovitis. In infections of direct origin, puncture wounds occurred in 37 per cent, lacerations in 18 per cent, compound dislocation and gunshot wounds in 1 per cent. In infections of indirect origin, puncture wounds occurred in 5 per cent, lacerations in 12 per cent,

TABLE 1—BACTERIOLOGY AND CLINICAL COURSE

	Origin	Cases	Septicæmic course		Tendon slough		Osteomyelitis		Final Case	
			Present	Absent	Present	Absent	Present	Absent	I	II
<i>Streptococcus hemolyticus</i>	Direct	51		14			20	11		
	Indirect								1	
<i>Streptococcus hemolyticus</i> , <i>Staphylococcus aureus</i>	Direct									
	Indirect	18		5			8	10		
<i>Staphylococcus aureus</i>	Direct									
	Indirect	10								
<i>Streptococcus hemolyticus</i> , <i>Staphylococcus aureus</i> , <i>Micrococcus species</i>	Indirect	6	6		6					
<i>Staphylococcus albus</i>	Direct									
<i>Staphylococcus aureus</i> , <i>Bacillus proteus</i> , <i>Staphylococcus</i>	Direct									
<i>Streptococcus hemolyticus</i> , <i>Bacillus coli</i> , <i>Bacillus subtilis</i>	Direct									
<i>Streptococcus hemolyticus</i> , <i>Staphylococcus aureus</i> , <i>Staphylococcus</i>	Indirect									

abrasions in 8 per cent, human bit and felon in 6 per cent each, contusions and burns in 3 per cent each, and bleb and septic callus in 1 per cent each.

The primary site of infection in 50 per cent of the cases was found to be in the transverse volar creases of the fingers where anatomically the tendon sheath is devoid of its fibrous layer. The distal volar crease was the site in 27 per cent of the entire series, the middle volar crease in 16 per cent, and the proximal volar crease in 7 per cent. The closed spaces of the fingers were the primary sites in 37 per cent of the cases, the distal closed space was the site in 17 per cent of the entire series, the middle closed space in 12 per cent, and the proximal closed space in 8 per cent. The dorsum of the hand was the site of infection in 12 per cent and the entire finger was the site in 1 per cent.

A most important factor influencing the end result is the time elapsed between the onset of infection and operation, or the delay in operation. However time is not the only important factor. Some hands operated upon within 24 hours did poorly while others operated upon after 5 days did well. In group 1 the bad results, the average time before operation was 6 days, the least time before operation 24 hours, the greatest time 11 days. In group 2 fair results, the average time before operation was 5 days, the least time before operation 48 hours and the greatest time 9 days. In group 3 the optimum results, the average time before operation was 3.3 days, the least time be-

fore operation 20 hours, and the greatest 15 days.

Table 1 is a summary of the bacteriology of clinical course in the 100 cases.

As to complications 1 patient died of pulmonary embolus and a second patient from thrombosis. A second patient the septic tenosynovitis was complicated by diabetes. These deaths make a mortality rate of 3 per cent.

Osteomyelitis or stiff fingers caused by osteomyelitis or septic arthritis made it necessary amputate in 18 per cent of the cases. Tendon slough was the most common cause of amputation and occurred in 41 per cent of cases. Osteomyelitis was relatively common and occurred in 18 per cent of the cases. Involvement of the closed space occurred in 18 per cent of the cases. Tenosynovitis of the thumb, index, and middle fingers. 12 of the 18 cases the origin was in middle finger. The middle palmar space involved in 10 per cent of the cases from tenosynovitis of the ring, little and middle fingers. Incidentally in 2 of the 3 cases the origin of the middle palmar space the origin was in middle finger. Septic tenosynovitis of the middle finger may be complicated by either deep abscess or middle palmar space abscess. In one case did a deep fascial space abscess spread to forearm. Adhesions about tendons caused limited function was a complication in 10 per cent of the cases. Septic arthritis was found in 10 per cent of the cases. Lumbar space abscess occurred in 9 per cent of the cases.

Involvement of the tendon sheath of the thumb occurred in 18 per cent of the cases. In 10 per cent of the entire series, the radial bursa became involved from tenosynovitis of the thumb, and 8 per cent of the entire series both radial and ulnar bursae became involved from tenosynovitis of the thumb. Tenosynovitis of the little finger occurred in 6 per cent of the cases. In one half of this group, or 3 per cent of the entire series, the ulnar bursa became involved. In 2 per cent of the entire series both ulnar and radial bursae became involved from tenosynovitis of the little finger. In no case was there a spread of infection from the tendon sheath of the thumb from an original infection in the little finger.

In 3 per cent of cases there was a spread of infection to the space in front of pronator quadratus muscle in the wrist. In each of these cases tendon slough, radial and ulnar bursitis, and osteomyelitis occurred. In each case pus was found in the flexor carpi radialis tendon sheath and in the wrist joint. It cannot be definitely stated whether the spread to the wrist joint was by direct extension or via the sheath of the flexor carpi radialis tendon.

In 3 per cent of cases infection spread to the forearm spaces. In each case tendon slough, osteomyelitis, and infection of both radial and ulnar bursae occurred. In each case pus spread up the forearm into the space formed by the flexor digitorum sublimis muscle anteriorly and the flexor digitorum profundus and flexor pollicis longus muscles posteriorly.

Table II gives a comparison of end-results reported by several surgeons. A review of the literature reveals that, in the past 30 years, little progress has been made in securing better end-results in the treatment of acute septic tenosynovitis of the flexor tendons of the hand.

TABLE II—END RESULTS

	Group 1 Bad Per cent	Group 2 Fair Per cent	Group 3 Optimum Per cent
Keppler (Berlin) 1912	28	10	62
Schlessl (Bardenberg) 1925	28	14	57
Deicke (Leipzig) 1933	53	17	30
Brinnell (New York City) 1938	50	22	28
Present series	47	20	33

#### ANATOMICAL STUDIES AND SURGICAL TREATMENT

A mixture of 1 part of bismuth subnitrate, 1 part of cotton seed oil, and 2 parts of petrolatum may be injected, by the open method, into the tendon sheaths and the radial and ulnar bursae, and x-ray studies then made. By this method the comparative position of pus accumulations may



Fig. 1 Tendon sheaths of the radial and ulnar bursae injected with radiopaque material showing comparative position of pus accumulations

be visualized. It is of value in determining the location and direction of incisions (Fig. 1).

A knowledge of the surface anatomy and deeper structures of the hand is basic for the proper treatment of septic tenosynovitis. An understanding of the muscles, blood vessels, and nerves, particularly in their relationship to the tendon sheaths of the thumb and little fingers, is of great importance. A knowledge of the anatomy of the wrist and the spaces of the forearm, especially in relation to radial and ulnar bursae, is of much practical importance.

General anesthesia is always used. A blood pressure cuff is used for a tourniquet.

On the index, middle and ring fingers the middle and distal volar transverse creases extend to a point about half way between the anterior and posterior surfaces of the finger, on the medial and lateral aspects. The proper digital arteries are



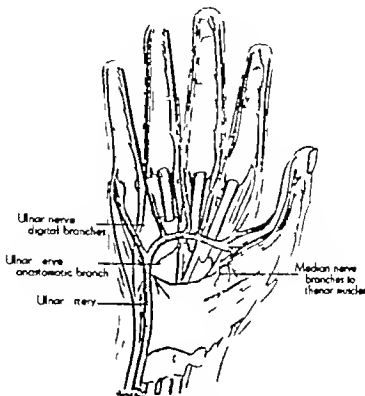


Fig Drawing showing median and ulnar nerves and ulnar artery

slightly posterior to the digital nerves, and are found at the level of the anterior third of the medial and lateral aspect of the fingers.

Auchincloss has shown that digital arteries give off branches which form an anastomotic arch of blood vessels in the anterior subtendinous space. This anastomotic arch gives off vessels to supply bone, synovial membrane of joint and of tendon sheath, and the tendon itself. The tendon receives its branches through the mesotenons or so called ligamenta brevia.

In the surgical treatment of infections of the index, middle and ring fingers several points may be emphasized.

Incisions should drain every pocket of pus. Interrupted incisions over the medial and lateral aspects of the proximal and middle phalanges have been used and discarded because drainage was incomplete. In too many instances secondary incisions were required and the incidence of tendon slough was too great.

Auchincloss has suggested the use of truncated flap incisions including all tissue down to the tendon sheath. In this incision, the distal end is

cut along the flexion crease. The medial or lateral parts of the flap are cut obliquely downward, the digital vessels and nerves are saved, and the incision is extended nearly to the proximal crease. These incisions have been made over the proximal and middle phalanges. Rubber tissue and thread have been used for operative drainage. The incision affords excellent exposure of the sheath but, in this clinic, the subsequent sloughing of tendons has been great. The exposure of the tendon may be too extensive. Also I have noted rolling backward and sloughing of some of the distal part of the tendon and this delays healing.

Medial or lateral longitudinal incisions extend from the base of the distal phalanx to the level of the proximal or distal digital crease and are placed anterior to digital vessels and nerves, but are not used. These incisions are condemned because they necessitate cutting across the digital crease and this procedure endangers the vessels and nerves and may lead to herniation of tendons.

In this clinic the lateral incision has proved of greatest value. It extends from the distal crease

the proximal volar crease. The incision is posterior to the lateral extensions of the volar transverse creases, and is posterior to the digital vessels and nerves. The only objection I find to it is that it involves cutting that branch from the digital artery which makes up part of the anastomotic arch of blood vessels in the anterior subcutaneous space, from which the mesotenon is supplied. However, this small cut branch is not an end artery, and I believe that anastomotic circulation from the other side may be adequate to nourish the tendon sheath and tendon. This incision is followed by the least slough and provides adequate drainage. The sheath is nicked, a groove director is inserted, and the sheath is cut to the entire length of the skin incision. In almost all cases of septic tenosynovitis of the flexor tendons of the index, middle, or ring fingers, it is necessary to drain the palmar portion of the tendon sheath. This is accomplished by a longitudinal incision from the base of the proximal digital crease and carried about 2 centimeters proximally into the palm. The incision is begun on the same side of the digital crease as is the digital incision. The incision in the sheath joins that made over the digital portion. With index and ring finger infections the digital incision may be on the medial or lateral aspect of the finger. With tenosynovitis of the middle finger, the digital incision may be made on the medial or lateral aspects of the finger. If there is a complicating thenar space abscess, the incision should be on the lateral aspect. If there is a complicating middle palmar space abscess, the incision should be made over the medial aspect of the finger. In this series, 2 cases of tenosynovitis of the middle finger were complicated by thenar space abscess, and 2 cases were complicated by middle palmar space abscess (Fig. 4).

The sheath of the flexor tendon of the *little finger* extends from the base of the distal phalanx to about the metacarpophalangeal joint. On rare occasions, it may end there. However, it usually continues proximally in the form of the ulnar bursa.

The digital branches of the ulnar nerve to the adjacent sides of the ring and little fingers cross from the medial to the lateral side of the *ulnar bursa* at a point about 1 inch proximal to the metacarpophalangeal joint (Fig. 2). The anastomotic branch from the ulnar nerve to the median nerve crosses the fifth flexor tendon about 1.5 centimeters from the distal edge of the volar carpal ligament (Fig. 2). The ulnar artery, just before turning laterally to form the superficial volar arch, crosses the flexor tendon of the little



Fig. 3 Pronator space and interflexor space showing muscular boundaries and attachments.

finger, just anterior to the anastomotic branch of the ulnar nerve (Fig. 2).

In the surgical treatment of infections of the little finger and palmar portion of the ulnar bursa the following steps are followed:

A longitudinal digital incision is made over the lateral aspect of the little finger, posterior to the digital vessels and nerves and posterior to lateral extension of the volar digital creases. If there is no continuity between tendon sheath and ulnar bursa, or if there is an obstruction to the spread of infection by the products of infection in the region of the metacarpophalangeal joint, there may be no need for carrying the incision into the ulnar bursa. However, it is necessary to drain the palmar prolongation of the tendon sheath. This is accomplished by making an incision about 2 centimeters long from the center of the volar aspect of the proximal digital crease into the palm (Fig. 4).

Clinical evidence usually reveals whether the palmar portion of the ulnar bursa should be incised. In this series one half of the cases of tenosynovitis of the little finger were complicated by ulnar bursitis. However, if there is a question it is wiser first to cut into the septic tendon sheath and then to exert pressure over the ulnar bursa, proximally. If pus is obtained with pressure, the incision is carried into the ulnar bursa. The palmar portion of the ulnar bursa is drained by an incision extending from a point just proximal to the distal transverse crease in the palm, to about the apex of the triangle in the base of the palm. This incision is over the lateral edge of the hypothenar eminence (Fig. 4). The digital branches of the ulnar nerve, about 1 inch proximal to the metacarpophalangeal joint, and the anastomotic branch of the ulnar nerve to the median nerve and ulnar artery, about 1.5 centimeters distal to the distal edge of the volar carpal ligament, must be identified and must be retracted medially (Fig. 2).

As to the anatomy of the thumb and palmar portion of radial bursa, the sheath of the flexor

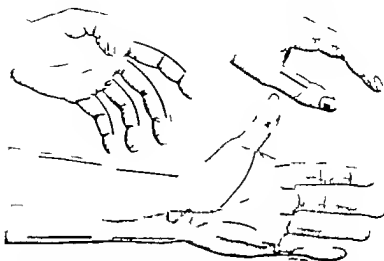


Fig. 4. Incisions for draining infected tendon sheaths, radial and ulnar bursae, spaces in wrist and forearm. Dotted line represents rarely used incision.

pollicis longus tendon extends from the base of the distal phalanx to about the middle of the first metacarpal bone, where it rarely ends. Usually it continues proximally beneath the volar carpal ligament, as the radial bursa ending about 4 centimeters above it. At the level of the first metacarpophalangeal joint, the tendon sheath of the thumb lies between the head of the adductor pollicis medially and the flexor pollicis brevis laterally (Fig. 1).

At about the level of the middle of the first metacarpal bone, a branch of the median nerve divides to send a branch to the medial and lateral aspects of the thumb (Fig. 2). The important motor nerves to the opponens pollicis, abductor pollicis brevis, and lateral portion of flexor pollicis brevis which rotate the thumb arise from this branch of the median nerve usually about 3 centimeters proximal to the digital branches (Fig. 2). At this level the tendons of the thumb lie between the two bodies of the flexor pollicis brevis. All these structures must be identified

otherwise the patient may be left with an insensitive thumb and one which cannot be rotated. In this series, the thumb flexor tendon sheath was involved in 8 per cent of cases, and the radial bursa was involved in 10 per cent of the entire series.

In the surgical treatment of infections of the thumb it should be noted that the thumb should be placed in a position of abduction before an incision is made to obviate anatomical distortion, particularly of nerves. A longitudinal digital

incision is made from the base of the distal phalanx to the base of the thumb, on the ulnar side. The palmar incision is separate from which starts at about the middle of the proximal volar crease just below the center of the distal aspect of the thumb. The incision is then curved over the medial aspect of the thenar extending about two-thirds the distance to the base of the thenar eminence. An incision is made into the sheath with care to avoid the sensory and motor branches of the median nerve. The portion of the radial bursa, proximal to where the nerves to the thenar muscles are found, is not drained and the volar carpal ligament is cut. The distal three-fourths of the volar carpal ligament is cut in 2 cases in this series, not to expose the radial bursa but to relieve pressure and to avoid injury to median nerve and flexor tendons. Incisions through the entire volar carpal ligament should not be made because of the exposure of tendons and the prolapse of tendons (Fig. 4).

The radial and ulnar bursae are in close proximity beneath the volar carpal ligament. Anatomically these bursae sometimes communicate. Clinically it should be assumed they always do. In the present series 10 per cent of the entire group involved the radial bursa from tendon sheath infections of the thumb. From ulnar bursa infections, 80 per cent spread to involve the ulnar bursa.

Pus accumulations in radial and ulnar bursae may rupture into the space bounded posteriorly by the pronator quadratus muscle and anteriorly

the flexor digitorum profundus and flexor ulnaris tendons in the wrist (Fig 3) In this series there was no tendency for the space in the middle palmar space abscesses to rupture into the space.

From the wrist pus spreads up the forearm into the space bounded anteriorly by the flexor digitorum sublimis, and posteriorly by the flexor digitorum profundus and flexor pollicis longus. Dissection of the muscles of the forearm reveals that this is true (Fig 3). The flexor digitorum profundus and flexor pollicis longus have their origin from the ulna, radius, and interosseous membrane from a point at the upper level of the pronator quadratus to the level of the oblique line of the radius. At the oblique line of the radius the flexor sublimis takes origin (Fig 3). Thus, anatomically, pus cannot extend up the forearm behind the flexor digitorum profundus and flexor pollicis longus. It must spread anterior to these muscles. In the upper forearm the spread of pus is blocked by the origin of the flexor digitorum sublimis and pronator quadratus (Fig 3). In its course pus spreads over the deeper muscles almost to the radial vessels on the lateral side, and beyond the ulnar vessels on the medial side.

If both ulnar and radial bursae are involved, and if pus has ruptured into the pronator quadratus space in the wrist, an incision on the ulnar side of the wrist may be adequate. A 2.5 inch incision is made at the anterior surface of the ulna, about 1 inch above the styloid of the ulna. The approach is behind the flexor carpi ulnaris and ulnar vessels. When the deep fascia is incised, the bulging ulnar bursa may be seen in the wound.

If the radial bursa alone is involved, an incision over the radial side of the wrist is made. A 2.5 inch incision is made over the volar lateral aspect of the radius, as close to the bone as possible, and posterior to the radial artery. When deep fascia is incised, the bulging radial bursa may be seen in the wound (Fig 4).

Usually no drain is necessary for radial and ulnar bursae incisions, if the incision is sufficiently long. If great edema is present, a rubber tissue drain is inserted for 24 to 48 hours.

Most of the infections from the wrist tend to spread up the ulnar side of the forearm where most of the flexors are.

With infection of the intermuscular space of the forearm, a 2.5 inch incision is made between the flexor carpi ulnaris and the ulnar margin of the flexor digitorum sublimis. The ulnar margin of the flexor digitorum sublimis is retracted

laterally, and the space between it and flexor digitorum profundus is entered by blunt dissection toward the profundus. Great care should be taken not to injure the ulnar nerves and vessels which are adherent to the under surface of the sublimis (Fig 4).

The incision over the ulnar surface of the forearm together with the wrist incisions is usually adequate. However, with extensive accumulations of pus, an incision is made over the radial side of the forearm. This incision is about 2.5 inches long along the outer edge of the flexor carpi radialis. At this point, the lateral edge of the flexor digitorum sublimis muscle can be identified, retracted inward, and the space entered by blunt dissection. The approach is internal to the radial artery.

**Sulfonamides** Sulfonamides were used locally and parenterally. Certain factors should be understood in the intelligent use of the sulfonamides locally. The toxic action of sulfonamides on cells, when used locally, is not a big factor in influencing the selection of the drug. Lyons has suggested factors which should be kept in mind when selecting sulfonamides for local application, namely: rate of absorption, persistence of crystalline drug, persistence of drug by chemical test, excretion of drug, diffusion in wound, and tolerance for inhibiting substances. Sulfanilamide is absorbed more rapidly, excreted more rapidly, and persists as crystals and chemically in the wound for the shortest length of time and is more soluble in serum than other sulfonamides. Sulfathiazole, sulfadiazine, and sulfapyridine follow in decreasing solubility as mentioned. Sulfanilamide has the greatest rate of diffusion in wounds. Next in order, in rate of diffusion, are sulfathiazole, sulfadiazine, and sulfapyridine. Dead tissue slows the rate of diffusion through the tissues. Even in dead tissue, sulfanilamide diffuses more rapidly than do other sulfonamides.

Sulfonamides are bacteriostatic and not bacteriocidal. Theoretically, sulfonamides are supposed to act by interfering with bacterial enzymes concerned in some way with nutritive substances. Sulfonamides compete for bacterial enzymes with an essential metabolite, described as a substance or chemical group which takes an essential part in a chain of syntheses necessary for bacterial growth. Sulfonamide inhibition results from an excess of essential metabolite. MacLeod showed inhibitor substances in fresh muscle extracts and pus.

Sulfanilamide, sulfathiazole, and sulfadiazine have been used in this series. Locally these drugs have been applied as a light dust to in-

ected surfaces in a dose of about 1 gram per 10 square inches of surface as suggested by the subcommittee on surgical infections of the National Research Council. Sulfanilamide has been used with hemolytic streptococci alone, or in mixed infections. Sulfathiazole has been used with staphylococci in single or mixed infections. Sulfadiazine has been used more recently for hemolytic streptococci, staphylococci and all mixed infections. Recent clinical observations indicate that sulfadiazine may be the drug of choice. Sulfadiazine may have a superior tolerance for the local inhibitors.

Since the advent of sulfonamide treatment in purulent tenosynovitis there has been no great decrease in the incidence of tendon slough. This fact, I believe is due to the time factor. With septic tenosynovitis existing for 48 to 72 hours, it is quite obvious that the sulfonamides cannot be a great factor in correcting physiological changes which have occurred particularly in blood vessels, or in correcting pathological changes in the involved tissues, or in correcting the mechanical changes in the tendon sheath.

Despite the fact that there has been no appreciable change in the incidence of sloughed tendons with sulfonamide therapy, there has been a decided decrease in the incidence of other severe complications in septic tenosynovitis. The decrease is noted in the incidence of osteomyelitis, thenar space abscess, middle palmar space abscess, ulnar bursitis, infections of the pronator quadratus space in the wrist, and the interosseous space in the forearm. If sulfonamide therapy is started early enough, it will undoubtedly be a factor in decreasing incidence of tendon slough. The marked decrease of severe complications of septic tenosynovitis with sulfonamide therapy is comparable to the decrease in mastoiditis with sulfonamides in this media.

#### POSTOPERATIVE TREATMENT

The infected hand should be elevated on a pillow at all times to facilitate venous and lymphatic drainage. During the stage of acute infection, the hand and wrist are immobilized in an aluminum splint, in a position of function. Early postoperative motion was instituted in a group in this series, but aggravation of the infection in almost every case was seen. It is strongly advised to permit no motion until the infection is controlled. However with a sloughed tendon in the absence of osteomyelitis or septic arthritis, the joints may be manipulated to prevent adhesions, and permit future tendon grafting. Hot soaks are advised under aseptic conditions. If incisions are de-

quate, rubber tissue drains may be soaked 4 to 6 hours. Many cases of septic tenosynovitis which have been doing well in the hospital have been discharged to the Out Patient Department, as tendon slough occurs. This, I believe is the result of permitting the patient to be ambulatory before the infection has subsided. Contamination of the wound, after discharge from hospital, has also occurred. Hospitalization of patient until the infection has subsided is of paramount importance.

#### SUMMARY

In 100 cases of acute septic tenosynovitis of the hand, the origin of infection was either by direct or indirect inoculation. In no case was there evidence of hematogenous or lymphatic origin.

On the basis of function, results may be classified in three groups, bad, fair or optimum.

Etiologically there were four outstanding factors: trauma, location of trauma, time of bacteriology. Puncture wounds are the most common types of injury. Puncture wounds, particularly at the volar digital creases, caused the most serious infections. The thumb, index, and middle fingers were most frequently involved.

Time, or delay in operation, is the biggest factor in producing poor results. The average time before operation in group 1 was 6 days; in group 2, 5 days; and in group 3, 2.3 days.

In the group of cases in which the hemolytic streptococcus alone or combined with the bacilli caused the infection, the results were poor. In the group in which the Staphylococcus aureus caused the infection, the results were best, and in all the mixed infection cases the results were poor.

The mortality was 2 per cent. Amputations were performed in 18 per cent. Tendon slough, the most common cause of poor results, occurred in 42 per cent. Osteomyelitis was found in 35 per cent. Thenar space abscess occurred in 12 per cent and middle palmar space abscess in 10 per cent. Tendon adhesions caused limited motion in 10 per cent. Septic arthritis was found in 9 per cent, and lumbal space abscess in 9 per cent. Tenosynovitis of the thumb involved in 10 per cent spread to the radial bursa occurred in 10 per cent of the entire series, and from the wrist to the ulnar bursa in 8 per cent of the entire series. Tenosynovitis of the little finger occurred in 10 per cent with a spread of the infection to the ulnar bursa in one-half of the number of cases, or 3 per cent of the entire series, and to the radial bursa from the ulnar bursa in 2 per cent of the entire series. The pronator quadratus space at the wrist was involved in 3 patients and the knee

flexor space in the forearm in 3 per cent of the entire series

The average stay in the hospital was 19.9 days

Results were generally poor 47 per cent were in group 1, the bad results, 20 per cent in group 2, the fair results, and 33 per cent in group 3, the best results. Results in this series are no better than those reported 30 years ago and those reported by others

# CONCLUSIONS

The greatest hope for improvement in results lies in the early treatment of suppurative tenosynovitis and the proper observation of wounds of the fingers. Puncture wounds, at the digital creases in particular, should be considered as predisposing to suppurative tenosynovitis

Extreme care not to change bacterial flora from a single strain to a mixed infection is of great importance. This danger is avoided by exercising strict aseptic precautions at the time of operation and particularly at the time of postoperative dressings

Incisions should be adequate to drain every pocket of pus. Inadequate incisions invariably necessitate subsequent incisions and lead to poor results. Incisions may provide too much exposure to the tendons and thus produce a tendency to tendon slough or occasionally herniation of the tendon. Before an incision into a tendon sheath is made one must have a thorough knowledge of the surgical anatomy of blood vessels, nerves, and neighboring muscles. A clear knowledge of the pathway of pus in tenosynovitis is also basic. Rubber tissue drains may be used but are usually discarded in 24 to 48 hours

The knowledge that an infection in any tendon sheath may complicate the treatment of an injury

to the hand or fingers should make one alert to discover this complication early

Sulfonamides, with sulfadiazine in particular, when used at an early stage, parenterally and locally, are of real value in decreasing the incidence of severe complications

After operation, the hand should be elevated on a pillow to aid lymphatic and venous drainage. Active motions should be avoided until the infection subsides. The hand should be placed in an aluminum splint in a position of function. Dressings and soaks are performed with strict asepsis. With tendon slough but in the absence of osteomyelitis or septic arthritis, manipulation of the fingers is performed to prevent adhesions and to permit future tendon grafting. The patient should be hospitalized until the infection subsides

# REFERENCES

1. AUCHINCLOSS, H. *Surgery of the Hand*, Nelson Loose Leaf Surgery, 3, 459, 1927
2. BELLONE, A. *Arch radiol*, Nap, 1939, 15 491-495
3. CLEVELAND, M. *Arch Surg*, 1925, 7 661
4. COLONNA, P. C. *Am J Surg*, 1940, 50 509
5. DEICKE, H. *Beitr klin Chir*, 1933, 158 461
6. FILDES, P. *Lancet*, Lond, 1940, 1 955-957
7. FORSELL, W. *Nord med Ark Stockholm*, 1903, hft 3, No 14 1, hft 4, No 19 55
8. GARLOCK, J. H. *Surg Gyn Obst*, 1924, 39 165
9. GRINNELL, R. S. *Ann Surg*, 1937, 105 97-110
10. HAWKING, F. *Lancet*, Lond, 1941, 1 786-788
11. ISELIN, M. *Schweiz med Wschr*, 1932, 13 1159
12. KANAVEL, A. B. *Infections of the Hand*, 7th ed Philadelphia Lea & Febiger, 1939
13. KEEPLER, W. *Ztschr Chir*, 1912, 115 63
14. KOCH, S. L. *Ohio M J*, 1938, 34 1325-1328
15. LYONS, C., and BURBANK, C. *Surg Gyn Obst*, Internat. Abstr Surg, 1942, 74 571
16. MACLEOD, C. M. *J Exp M*, 1940, 72 217-232
17. POIRIER, P. *Traité d'anatomie humaine* Paris Masson et cie, 1896
18. SCHIESSL, M. *Münch. med Wschr*, 1925, 72 1728

# THE MODIFIED MIKULICZ RESECTION FOR CARCINOMA OF THE COLON

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THE historical development of the type of resection of the colon introduced by Bloch and developed by Paul and Mikulicz has been adequately reviewed elsewhere. Rankin's modification of the Mikulicz technique removed the serious objections to it. We believe that the reported recurrences of carcinoma in the abdominal wound following the original Mikulicz procedure were the result of extension of the growth from adjacent mesenteric glands which were not resected. One no longer sees these recurrences when the gland bearing mesentery is adequately removed.

Certain objections to the modified Mikulicz resection have been raised: first, that the gland bearing mesentery cannot be adequately resected; second, that this type of resection requires prolonged hospitalization; and third, that the mortality is high. In retrospect our experience with the Rankin modification seemed very satisfactory and led us to review a recent series in detail.

From January, 1938, to July, 1942 the senior author resected 77 lesions of the transverse and left colon by the modified Mikulicz technique. The distribution of these was as follows: sigmoid colon, 58; descending colon, 3; splenic flexure, 6; and transverse colon, 10. The pathological diagnosis in 71 cases was adenocarcinoma, and in one case each lymphosarcoma, endometrioma, obstructing diverticulitis, segmental ulcerative colitis with obstruction, megacolon, and a curious cystic degeneration of the collagenous fibers with ulceration of the mucosa in a two foot segment of a greatly elongated sigmoid.

Preliminary cecostomy for the relief of acute or subacute obstruction was done in 10 cases, or 13 per cent. Cecostomy was done once at the time of resection because of a coexisting diverticulosis of marked degree. The colostomy was closed as a secondary procedure in 66 cases. Spontaneous closure occurred in 11 cases, or 14.3 per cent of the series. Five or 6.3 per cent, of the 77 patients died in the hospital, 3 of peritonitis and 2 of pneumonia.

## TECHNIQUE

The technique of resection in this series was essentially that of the Rankin obstruction opera-

tion with a few modifications of the original description. The colostomy in each case was brought out through a vertical incision.

We wish to emphasize certain technical details which are important from the standpoint of both the cure of cancer and the reduction of mortality and morbidity. Mobility of the lesion to be resected determines whether this operation can be done. This mobility must be sufficient to meet two cardinal points: first, the wide resection of adjacent mesentery; and, second, the proper formation of the double-barrelled colostomy. It is essential that the arms of the colostomy fall together to form a good spur without axial or torsional tension. The arms may be maintained in position by suturing together several appendices epiploicae, but the colon itself is never sutured, neither serosa to serosa, nor serosa to any part of the abdominal wall.

If the mesentery of the involved loop of colon is short, or if for any reason mobility is not sufficient, it is better to do a resection and stoma with complementary cecostomy or colostomy than to attempt a Mikulicz resection which might be inadequate for the cure of cancer and hazardous because of tension on the colostomy.

In the formation of the colostomy care must be taken that the mesenteric borders of the bowel arms are placed in such a position that the peristaltic waves will not crush the blood supply.

During the time that the Rankin clamp is in place we do not hesitate to passing a catheter into the proximal loop of the colostomy at the first sign of distention of the loop, or at the onset of generalized abdominal distention or cramps. The Rankin clamp is usually removed on the fifth postoperative day and the upper clamp is applied immediately. To be satisfactory the upper clamp must crush without cutting and must not be tightly in the axis of the colostomy. It should be removed as soon as it feels loose to gentle touch. The position of the clamp should be inspected twice daily. After removal of the clamp, it is well to allow at least 48 hours to elapse before the colostomy is examined digitally since otherwise the sealed edges of the bowel may be disturbed intraperitoneally.

Closure of the colostomy should be a simple procedure, and the wound should heal promptly with only occasional transient fecal leakage, provided certain details in technique are observed. Sufficient time must elapse between resection and closure to allow the induration of the tissues about the colostomy to subside entirely. Ten weeks is the optimum interval.

The colostomy should be well mobilized and freed of its attachment to the fascia down to the peritoneum. It does not matter if the peritoneal cavity is actually entered, since local tissue immunity prevents any peritoneal reaction. The bowel must be trimmed of adherent fat and the rim of scar tissue about the stoma excised. The freshened edges of the bowel are sutured transversely with two rows of fine catgut. We prefer to close the fascia with interrupted alloy steel wire sutures and the skin and subcutaneous tissues with alloy steel wire vertical mattress sutures. Several small gauze wicks are placed beneath the fascia between the interrupted sutures.

With this technique patients are allowed out of bed on the 6th postoperative day and are discharged from the hospital on the 7th day. In this series of cases it has never been necessary to close a colostomy a second time.

Spontaneous closure of the colostomy saves the patient time and, in this respect, is desirable. Whether or not spontaneous closure occurs depends on how far below the skin edge the bowel retracts. Most of the colostomies in this series of cases were brought well out to the skin edges without tension, became adherent to the skin, and therefore necessitated closure. Occasionally, a mortality will occur from retraction of the loops under tension, and we believe that morbidity and mortality are decreased when the bowel loops are well mobilized and in full view at all times.

#### ANALYSIS OF STUDY

The Mikulicz type of resection may be applied to any portion of the colon sufficiently mobile to allow adequate resection of the adjacent gland bearing mesentery and the formation of an adequate colostomy. Since early in 1938 this operation has been preferred to resection with anastomosis in instances in which either of the two procedures might be indicated. The mortality for the Mikulicz procedure is low, and the morbidity is minimal. Furthermore, when the involved colon is mobile enough, the operation for the cure of cancer is as adequate as resection with anastomosis. The extent of resection in both types of operation is delineated by the blood supply in the same manner.

The Mikulicz procedure has been objected to on the grounds that it is a stage operation, and that it requires prolonged hospitalization not only for the resection but also for the closure of the colostomy. This need not be so, and in our experience the total duration of disability is only slightly longer than that following resection with anastomosis. In this series the average hospitalization for resection from the day of admission was 28 days. This figure includes preoperative preparation in all cases and 10 cases in which preliminary cecostomy was necessary for decompression. The average hospitalization for the closure of the colostomy was 8 days.

For a long time the senior author has advocated one stage operations in surgery of the colon. The closure of the colostomy according to the aforementioned technique has been uniformly successful and has earned with it so little morbidity and inconvenience to the patient that we no longer look upon it as a stage of an operation. Certainly the Mikulicz procedure cannot be placed in the same category as a two stage combined abdominoperineal resection or a two stage resection of the right colon.

We prefer this procedure for lesions of the distal two-thirds of the transverse colon, the splenic flexure, and the left colon. For lesions of the right colon and those just distal to the hepatic flexure, a one stage ileocelectomy with end-to-side ileo-transverse colostomy has appealed to us as the best operation. The discharge of small intestinal contents after a Mikulicz operation on the right colon is discouraging to the patient, and the skin irritation is often difficult to control. In the poorer risk patients the loss of electrolytes and fluid from the ileum is not well tolerated. In addition the mortality of one stage ileocelectomy should not be greater than that of the Mikulicz operation.

There has been frequent discussion about the application of the Mikulicz resection to lesions at or near the "rectosigmoid junction." Apparently, there is no unanimity of opinion as to the location of this point. We consider the rectosigmoid junction to be a small segment of bowel beginning at the peritoneal reflection in the rectovesical pouch or cul-de-sac, extending proximally for not more than 2 inches. Most lesions at this point obviously cannot be exteriorized, and consequently ideas as to what constitutes the rectosigmoid junction must vary considerably.

Most lesions low in the sigmoid do not lend themselves well to this type of operation. Tension on the distal loop of bowel renders the procedure hazardous, and the amount of mesentery



resected is frequently inadequate. If the question arises as to the choice of procedure, we mobilize the bowel as in a combined abdominoperineal resection, preserving the blood supply however. If sufficient mobilization cannot be secured combined abdominoperineal resection is carried out. Although this necessitates a permanent colostomy the mortality and morbidity are so much lower than when alternative procedures are used in this area that the combined operation is justified.

#### CONCLUSIONS

1. From January 1938, to July 1942 77 modified Mikulicz resections were performed on the transverse and left colon. There were 5 hospital deaths, a mortality of 6.5 per cent.

2. The observation of certain technical points in the resection and closure of the colostomy reduces the mortality and morbidity.

3. In properly selected cases this type of section is as adequate for the cure of cancer as resection with anastomosis.

4. There are certain objections to its use in the right colon and in the lower sigmoid.

#### REFERENCES

- CHODURA, C. D. L. *Proc. Mayo Clin.* 311, 26, 37-542.
2. DIXON, C. F. *Proc. Mayo Clin.* 336, 47-48.
3. JONES, THOMAS E. *Surg. Clin. N. America*, 1939, 3-134.
4. LARRY, F. H. *Surg. Gyn. Obst.*, 93, 51 437-438.
5. *Idem.* *Ann. Surg.* 63, 1.
6. M'COY, C. W. and SAMPSON, W. C. *Ann. Surg.*, 1900, 430-436.
7. RANKIN, F. W. *Surg. Gyn. Obst.*, 93, 50 394-7.
8. *Idem.* *Surg. Gyn. Obst.*, 93, 50 410-414.
9. SAMPSON, W. E. T. *Ann. Surg.* 1902, 4 28-300.
10. STONE, H. B. and McLAUGHLIN, SAMUEL J. *Am. J. Am.* 1930, 3 252-253.

# VOLVULUS OF THE SIGMOID

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**V**OLVULUS of the sigmoid occurs when the sigmoid is so redundant and the mesentery so relaxed as to permit a twisting of this part of the gut. The obstruction may be partial, complete, or strangulated.

Clinically significant redundancy of the gut may be congenital or acquired. Too much sigmoid may be a congenital abnormality, we will report a case of a 3 months old infant in whom the congenital factor must have been the only important one. We will report also a case of a patient who died at the age of 93 years from a strangulated volvulus of the sigmoid. In the latter patient it seems reasonable to assume that while the sigmoid was probably congenitally overlong, enough redundancy to produce strangulated volvulus would not have been present in the abdomen for 34,000 days without having produced symptoms. A study of the literature and of my cases convinces me (D M) that redundancy may be increased over a period of years to the point where it will cause strangulated volvulus. While the sigmoid may be long enough to permit volvulus in early infancy, those persons with less sigmoid may at first develop a partial volvulus only. Relaxation caused by age and repeated attacks of partial volvulus will gradually lengthen the mesentery and sigmoid until attacks of complete obstruction are followed by strangulation. Thus, volvulus of the sigmoid follows the well known law that many congenital abnormalities of the abdomen do not become manifest until adult life.

The symptoms at first are attacks of partial obstruction of the colon. Obstipation for a day is followed by a more or less distended abdomen and gas pains below the navel. Patients say, "If I could only pass the gas I would be all right." Sometimes they do pass some of the gas and some of the feces but not enough to get complete relief, so the attack continues. In one of our patients the attacks lasted from 12 hours to 2 weeks. Freedom between attacks varies from days to years. The tendency is for the attacks to become more frequent and more severe until the terrific pain of complete obstruction or strangulation sends the patient to a doctor.

From the surgical and roentgenological services of the King County Hospital and Providence Hospital

Before obstruction occurs there may be tenderness on the left side and occasionally the redundant sigmoid may be palpated above the navel on the left side. It seems like a phantom cyst that disappears as it is being examined. X-ray examination at this time may not aid in diagnosis. Since one-third of all patients having barium enemas show some redundancy of the sigmoid, the roentgenologist may not usurp the clinician's rightful function of making diagnoses. The clinician likewise is apt to be thinking in terms of colitis, kidney disease, diaphragmatic hernia, or just nervous indigestion. Later, when hypertrophy of the redundant loop or obstruction has occurred, attention is directed to the sigmoid. When a patient has learned that an enema, especially one taken in the knee-chest position, will produce relief, recurrent volvulus of the sigmoid should be suspected.

The incidence of recurrent volvulus of the sigmoid is more common than the diagnosis. Bloodgood reported 1 case among 103 cases of intestinal obstruction. Hays reported 5 cases among 110 cases of intestinal obstruction and quotes Briggs in the *Ohio State Medical Journal*, 1912, as having stated that "volvulus of the sigmoid causes 15 per cent of intestinal obstructions." In the King County Hospital, Seattle, Washington, from 1934 to 1941 inclusive, 496 patients with intestinal obstruction were admitted. Of these cases the following 5 were due to volvulus of the sigmoid.

**CASE 1 (110-959)**, a woman 93 years old, was admitted March 16, 1938, with cyanosis and an irregular pulse. She was in a very critical condition and died 24 hours later. A distended abdomen with generalized tenderness but no masses was noted. At autopsy a diagnosis of gangrenous volvulus of the sigmoid with peritonitis was made. Volvulus had not been suspected before autopsy.

**CASE 2 (5149)**, a man 80 years old, was admitted November 11, 1937, with cerebral concussion and fractured ribs, he was irrational. Eighteen days later he was walking about the ward although he was confused mentally. He suddenly expired December 22, 1937. At autopsy by a coroner the findings were fractured left 2d, 3d, 4th, and 5th ribs, abscess of chest wall, abscess of left kidney, cerebral atrophy, and redundant sigmoid and volvulus with partial obstruction.

**CASE 3 (105053)**, a 28 year old Indian woman, was admitted October 4, 1937. An appendectomy had been done 1 year before and was followed in a month by several attacks of abdominal cramps and vomiting. The present attack was of 3 days' duration. The abdomen was distended

TABLE I.—SUMMARY OF CASES  
From the Records of King County Hospital

Sex	Age	Duration of symptoms	Surgical procedure	Result
F	31	Diagnosis at autopsy only	None	Discharged day after admission
M	86	Diagnosis at autopsy only	None	Discharged
F	18	Year or more	Simple reduction of volvulus	No follow-up
F	46	Before operation, unknown operation at least 1 year	Simple reduction of volvulus	Continuation of symptoms
F	600	Unknown	Simple reduction of volvulus	Reoccurrence of distention and death after surgery

Author's Private Cases at Providence Hospital

F	37	At least 1 year	Resection with primary end-to-end anastomosis	Symptoms due to 1 year, later death from unknown cause
F	51	Probably 1 year	Appendectomy and resection with primary end-to-end anastomosis	Symptoms due to 1 year
F	51	"For years"	Appendectomy and resection with primary end-to-end anastomosis	Symptoms due to 1 year
M		Years or more	Resection with primary end-to-end anastomosis	Symptoms due to 1 year
M	30	Years	Appendectomy and resection with primary end-to-end anastomosis	Walled from hospital day after admission. Bowel function nearly normal

and there was visible peristalsis, there was no tenderness or rigidity. A ventral hernia was present but it was not incarcerated. She had vomited only during the past 4 hours. She was operated upon the day after admission with simple reduction of the volvulus. She was discharged October 3, 1937 and there was no follow-up.

CASE 4 (3097) 20 years old, was admitted February 3, 1936. She had been admitted 3 months earlier and diagnosis of obstruction relieved by enemas as made. The second attack followed the absence of bowel movement the day before. She had cramp-like pains, distended abdomen, and tenderness and rigidity of the lower left quadrant with nausea. At operation the volvulus was untwisted and reduced. Postoperative recovery was normal, and she was discharged from the hospital February 8, 1936. She was admitted to the hospital total of 6 times before and after surgery and diagnosis of intraluminal obstruction or fecal impaction as made. She came to the out-patient department several times in 1940 with the same complaints.

CASE 5 (5896) 3 months old baby girl, was admitted October 7, 1931, and diagnosis of malnutrition with progressive abdominal distention was made. Acute intussusception was suspected on November 8, 1931. At operation the same day the symptoms were found to be caused by volvulus of the sigmoid. The volvulus was reduced, but the next day distention recurred and the baby died. There was no autopsy.

### TREATMENT

Treatment of this condition in the past has not been a signal success. In 4 of the 5 cases at the King County Hospital the diagnoses were not made until after death. Simple untwisting of the volvulus either with or without passing of a rectal tube may give temporary satisfaction to the surgeon, but who can say when the condition will recur (3)? Plastic operations either on the mesentery, or on the colon have variably failed.

Bloodgood's first case had 37 hospital admissions between 1890 and 1906 with 5 operations before the final cure. The surgeon is often astounded at the time of a second operation to find that there is no vestige of the carefully planned and painstakingly performed previous operation (4). The redundant sigmoid must be resected to effect a cure.

In the presence of acute obstruction, resection is usually considered hazardous. However, Hays resected sigmoid and did side-to-side anastomoses 4 times in the presence of obstruction. The ends of the colon were inverted and brought out through the peritoneum. All patients recovered, 2 with fistulas. This method is the technique used by Bloodgood. The modern technique is much more apt to do an obstructive resection in the presence of obstruction as advocated by Rankin. This type is end-to-end, safer and at the same time curative.

In the absence of obstruction I recommend end-to-end union. Even if obstruction is present it may be relieved by enemas in the knee-chest position and the bowel prepared for surgery. I believe that this procedure is as safe as operation in the presence of obstruction, provided that the abdomen is not silent, proving there is no strangulation, and ( ) the attempt to relieve the obstruction is not persisted in too long.

The principles of end-to-end suture of the colon were well described by Lockhart Mummery (4) in 1917 and reiterated in 1935 (5), 21 years later. Further study of the blood supply of the colon



Fig 1 Case 1 Flat plate taken during pyelogram. Note large redundant loop filling almost entire left side of abdomen. Significance was not realized at time of examination.



Fig 2 Case 1 Roentgenogram taken after barium enema, showing large redundant loop of sigmoid. Note increased capacity of proximal colon.

(Steward and Rankin) and its clinical application (Metheny) makes the procedure even more certain. In my own 5 cases I used primary end-to-end anastomosis after resection of the sigmoid. During preparation the patient is given 1 gram of sulfanilamide every 4 hours for 36 hours just before surgery. An open technique is used, but it would seem the type of suture is not important provided the suture line is gas and water tight and does not impair the blood supply to the ends of the gut. The pad packing off the surgical field is moistened with metaphen. A continuous stitch of No. 00000 chromic catgut is first carried over and over, uniting the ends of the bowel. The serosal stitch is interrupted No. 60 cotton. A little sulfanilamide in Case 1 and sulfathiazole in Cases 2, 3, and 4 were placed around the suture lines as an added precaution. Postoperative distention is prevented by (1) continuous gastric suction through a Levine or Miller-Abbott tube, (2) prosthigmin, and (3) insertion of rectal tube every 4 hours. When the Miller-Abbott tube is used, liquids by

mouth are started the day after operation. Suction is discontinued on the 4th or 5th day. The reactions of my 4 patients were minimal and the last 3 left the hospital within 12 days after surgery.

**CASE 1** Miss N., 37 years of age, was first seen in September 1939. She had enjoyed good health until 1927 when she had a severe attack of pyelitis. After that attack she had been addicted to morphine and her health had not been good. In 1932 she had an attack of severe abdominal pain, diarrhea, anorexia, and weight loss of 5 weeks' duration, but no diagnosis was made. In 1935 she had a great deal of epigastric pain. After a gastrointestinal x-ray study a diagnosis of colitis was made, and hemolytic streptococcus was cultured from her stool. Diaphragmatic hernia was also considered a possible diagnosis. Beginning in 1937 alternating diarrhea and constipation with fatigue prevented her from working 50 per cent of the time. Abdominal distention came and went during this time. During the previous 3 months there had been many attacks of abdominal pain and tenderness. Physical examination was normal except for a temperature of 99.4 degrees and an indefinite but tender abdominal tumor, mostly above and to the left of the navel. She returned to her home town for further examination.

Ten days later she came back and was placed in the Providence Hospital. Staphylococcus albus and non-hemolytic streptococcus were cultured from her urine, but an intravenous urogram was normal. X-ray at this time (Fig. 1) showed gas-distended intestines and close inspection



Fig. 3. Case. Artist's drawing of large redundant sigmoid at operation. Not increased diameter and hypertrophy of the bowel wall.

tion will reveal the large redundant loop of sigmoid. This was not noticed at the time, but barium enema (Fig. 4) revealed the true cause of her abdominal complaints. Dr. Nichols actually saw the redundant loop twist and cause partial volvulus under the fluoroscope. After several days' preparation the sigmoid (Fig. 5) as resected September 30, 1935, and end-to-end suture as easily done. Before resection the loop reached above the cecocolic cartilage and the walls are hypertrophied. Convalescence as marked by difficulty in controlling drug addiction, and small blister in the incision gave pure culture of hemolytic staphylococcus. This blister looked as though it might develop into phagedenic ulcer but fortunately it healed promptly with the administration of neoprontol intra-muscularly.

This patient, as seen many times after her operation and she always said that she had no more abdominal distress (Fig. 4) and that her bowels moved normally. She is still morphine addict. On September 2, 1935, telephone call from the Wrist Cross stated she had been admitted to the Northern State Hospital at Sedro Woolley, Washington. She had been going without morphine for weeks and had gained 5 pounds. At 4:00 p.m. September 9, 1935, she is normal, at 4:30 p.m. she complained of gas pains, at 7:00 p.m. she is admitted to the infirmary and given morphine, 10 to 5 p.m. she is in shock, and at 10:00 p.m. she is dead. No postmortem examination as made.

CASE. Miss R, 3 years of age, as seen February 2, 1935. In 1935 she had high fever blood count leukocytosis. The diagnosis was colitis and after she had been careful to void rosin and after thought that fatigue made her colitis one. In 1935, she had an attack of influenza and peritonitis.



Fig. 4. Case. Roentgenogram taken after barium enema done. Smooth after operation. There is still 4 1/2 inch amount of space. Note absence of redundant loop.

and fever followed. Three weeks before coming to see it had severe abdominal pain that lasted for several weeks before breakfast. Four days before seeing me she had terrific steady pain in the lower abdomen. She called her doctor, he advised application of hot water bottle and the pain continued in 30 minutes. During the next hours she felt bloated and she belched but had no bowel movement. The next day she had normal movement.

Examination revealed nothing in particular except tender smooth, freely mobile mass between the umbilicus and cecocolic cartilage and there was blood in the stool. A barium plate x-ray of the abdomen (Fig. 5) was considered good, but closer inspection all show gas in the redundant loop in the upper left quadrant. A roentgenogram (Fig. 6) taken after barium enema on February 14, 1935, showed the redundant sigmoid. On February 20, 1935, after several days' preparation, an appendectomy and resection of the redundant sigmoid with end-to-end anastomosis of the colon were done. The redundant sigmoid had reached above the cecocolic cartilage. The operation was shown no abnormality except redundancy. The patient left the hospital March 4, 1935, day after surgery. A roentgenogram (Fig. 7) taken after barium enema March 9, 1935, showed absence of the redundancy.

CASE. Miss W, 3 years of age, had intermittent abdominal cramps for years. These cramps came in distinct attacks that lasted 7 to 10 days. They were associated with fever and vomiting and were entirely free of dyspepsia as long as several months and severe in the past.



Fig 5 Case 2 Flat plate of abdomen Note in upper left quadrant redundant loop of large bowel filled with gas

During physical examination on January 7, 1942, she was normal except for tenderness over McBurney's point. Report of the intestinal study was as follows: When an opaque meal was given there was no delay in the esophagus and the stomach filled smoothly and well. The position was much more to the midline and to the right of the midline than is usually seen, but there was no evidence of traction deformity. There was a large amount of gas in the transverse colon and descending colon, and this circumstance suggested that the displacement of the stomach was due to pressure from gas in the colon, although a part of such displacement may be congenital. There was no evidence of filling defect or abnormality and no delay in emptying. The cap filled smoothly and well. At the end of 5 hours there was no gastric residue, the head of the barium column was in the distal transverse colon which lay high under the diaphragm, and there was a large amount of gas present in this portion of the bowel and in the descending colon as well. The cecum was low in the pelvis and the terminal ileum appeared normal. The appendix was not seen. At the end of 24 hours there was barium throughout the colon with considerable residue in the cecum. Again the appendix could not be seen. An opaque enema (Fig 8) was given and there was no evidence of obstruction or gross filling defect, but the sigmoid was unusually redundant and elongated, extending upward almost to the diaphragm, apparently this was the portion of bowel which was displacing the stomach. The sigmoid then passed downward to join the descending colon in the left iliac fossa. The splenic flexure was unusually high and the capacity of the colon was about twice that of the average bowel.

On February 25, 1942, after several days of preparation, an appendectomy and end to-end suture of the colon were done after resection of the redundant loop. This loop easily reached above the ensiform cartilage before resection. The patient left the hospital March 8, 1942, 11 days after



Fig 6 Case 2 Roentgenogram taken after barium enema, showing large redundant loop of sigmoid. Note increased diameter of proximal colon



Fig 7 Case 2 Roentgenogram taken after barium enema, 1 month after operation. Note absence of redundant loop



Fig. 8 (left). Case 2. Roentgenogram taken after barium enema, showing large redundant loop of sigmoid. Note decreased capacity of proximal colon.

Fig. 9. Case 2. Roentgenogram taken after barium enema, 4 months after operation. Marked amount of spasm can still be noted in the region of left sacroiliac joint. Here the anastomosis is done. Patient is asymptomatic.

surgery. On March 27, 1932, another barium enema (Fig. 6) as given and the report as follows: "An opaque enema was given sufficiently to fill the distal colon, and there is no evidence of obstruction or gross filling defect. There was slight tendency toward spasm at the junction of the sigmoid with the descending colon, but this filled completely under the fluoroscope and there was no radiographic evidence of any permanent filling defect or abnormality. There was marked reduction in the length of the sigmoid as compared with the previous films."

CASE 4. Master W., 3 years old, was admitted to Providence Hospital March 1, 1932. Two years before he had had an attack of severe abdominal pain which had been diagnosed as left renal colic. The diagnosis had been made in the absence of hematuria or pyuria and in spite of the fact that no stone was found when the attack terminated. The pains had been so severe that renal colic was the only diagnosis considered. One year later an acute appendix had been removed but no other abnormality had been noted. For the past 3 months he had been unable to go to school. He had been having or attacks of severe pain daily in the left lower quadrant of the abdomen. The spasms of pain lasted for an average of 5 minutes. When asked to describe the attack he answered the statement that it felt as if something twisted. Asked if he could bear gasoline, he said, "No, but after the pain goes I can feel bubbles go by."

Physical examination revealed nothing remarkable. He was afebrile and undernourished. On palpation between

the navel and left superior iliac spine there was tenderness and increased resistance that seemed reflex. The liver, count, urinalysis, and pyelogram were normal, but roentgenogram (Fig. 10) made after barium enema revealed a redundant loop of sigmoid. The redundancy was not great as in any other 3 cases, but most significant was the fact that the barium enema reproduced the pain which he complained.

Operation as performed on March 18, 1932. There was a single adhesion between the cecum and the old abdominal scar, it was cut. There was slight amount of clear serous fluid in the pelvis. A large redundant loop of sigmoid was found. Its peritoneal sac was adherent by congenital band of peritoneum to the left lateral wall of the abdomen. The adhesion was cut, and the redundant loop was isolated and untwisted. About 10 inches of cecum were resected and end-to-end anastomosis was performed. Two days later he was out of bed, and 5 days after operation he was able to ride 20 miles home in an automobile. Four weeks after leaving the hospital he had gained 6 pounds and he was not only going to school but was able to help his father with the farm work.

CASE 5. M. S., 30 years of age, was first seen in consultation at the Providence Hospital May 8, 1932. He had been admitted to the hospital 5 days for abdominal pain and vomiting. His condition was diagnosed as appendicitis, but later the diagnosis was abandoned and he remained without any diagnosis until discharged. In 1935 he had several similar attacks and was readmitted to

the Providence Hospital for 10 days. He was in the hospital again for 10 days in 1939. A diagnosis was never made in spite of a roentgenogram (Fig 11) made in 1940 after a barium enema was given. This film shows marked redundancy of the sigmoid. For the next 2 years he had recurrent attacks of pain associated with obstipation, bloating, and borborygmus. The obstipation often lasted 5 or 6 days. During this time the abdomen would become distended and he had to unbutton his trousers and loosen his belt 2 or 3 notches. He learned that taking an enema sometimes terminated an attack. At one time he weighed  $4\frac{1}{2}$  pounds less after taking an effective enema.

Physical examination revealed an adult who was healthy and normal in every respect. All laboratory examinations were normal except for findings after the barium enema (Fig 12). The redundant loop of sigmoid was then twice the size it was 2 years before.

On May 22, 1942, 4 days later, resection of the redundant sigmoid and end-to-end union were performed followed by appendectomy. Seven days later he was out of bed and his bowels had moved spontaneously. He left the hospital May 31, 1942. It is too soon to evaluate the final result, but he should have no further trouble as his bowels have continued to act regularly and without trouble since his operation.

CASE 6 No 126735. The patient, a 65 year old man, was being treated at King County Hospital, Division No 2, for an ununited fracture of the right hip. About December 1 he had an attack of acute abdominal distention and pain with obstipation that was relieved after 12 hours by enemas. Following the acute attack he complained of gas pains every day. About 7 p.m. every night with massage of his abdomen, he expelled flatus and was relieved, but during the next day the abdomen would become slightly distended, he would again have cramps and again be relieved by the passage of flatus. He was admitted to Division 1 on my service (D.M.) the night of June 17, 1942. A diagnosis of acute low bowel obstruction was



Fig 10 Case 4. Roentgenogram taken after barium enema, showing redundant loop of sigmoid. Loop is not as large as in other cases, but has symptoms because the entire redundant loop swivels on the adhesions at its apex.



Fig 11 Case 5. Roentgenogram taken in 1940 which was interpreted as normal in spite of obvious redundancy of sigmoid.



Fig 12 Case 5. Roentgenogram taken 2 years later showing an increase in size of redundant sigmoid caused by recurrent volvulus.



made. The senior resident did blind rectostomy under local anesthesia. The patient's recovery was uneventful. X-ray examination, however, showed that instead of rectostomy sigmoidostomy had been done in a large redundant sigmoid. July 6, 1942, Dr. Wm. B. Hutchinson resected, in one stage, the sigmoid with its Sterna. The bowel was anastomosed end to end. Convalescence was uneventful. The patient was discharged September 3, 1942. There had been no further abdominal complaints and the wound fracture was healed.

**CASE 7.** A 6-year-old girl was admitted to my service (D.M.) at King County Hospital July 1, 1942. The temperature was 99 degrees and the leucocyte count 20,400 with 90 per cent polymorphous leucocytes. In spite of the admitting diagnosis of appendicitis, Dr. P. M. Kopera, who saw the child, wrote on the chart that the leucocytosis was out of proportion to the other symptoms. At the time of examination she was comfortable. There was some tenderness below McBurney's point, but no rigidity or bloating. Rectal examination showed tenderness on the right and there was blood on the examining finger. The mother stated that there had been many smaller attacks in the past 6 months. The attacks were characterized by severe pain, vomiting and fever. A ray examination of the colon on July 2, 1942, revealed a large redundant loop of the sigmoid. On July 20, 1942, the appendix and redundant sigmoid were removed, and primary end-to-end anastomosis was done. Convalescence was uneventful and the last note on her chart from the Out Patient Department on September 1, 1942, said "O.K. no complaints."

**CASE 8.** A C. P. 4-year-old boy was first seen in April, 1942, for loss of weight. He weighed 37 pounds and was 6 inches tall. He said he had lost 10 pounds in the past 6 months. No definite history could be obtained except that it hurt him to eat. On May 9, 1942, an x-ray diagnosis of redundant sigmoid with recurrent volvulus was

made. A high caloric diet as advised in the hospital, more fat in the stomach necessary would prevent attacks. In spite of all therapy he refused to eat and went to the Providence Hospital June 20, 1942, at which time he weighed 26 pounds. On July 2, 1942, the appendix and 8 inches of redundant sigmoid were removed. The

about 50 cubic centimeters of traumatic and redundant sigmoid reached almost to his knees. A period of end-to-end anastomosis. On the 5th postoperative he finished his lunch, escaped from the room and returned to his kitchen throughout the hospital and an untold amount of food. He had some abdominal pain that night and told me the next day that the operation had not helped him any. However, he was discharged from the hospital on July 2, 1942. An x-ray examination July 27, 1942, showed some spasm of the sigmoid but it was out completely and the sigmoid appears normal. Following the ray examination he had a more severe abdominal pain that I think was due to spasm. Following this he acquired confidence in himself and started eating normally. He was last seen November 2, 1942, he weighed 37½ pounds and stated that he could now remember he had had any abdominal distress and he felt all right.

#### REFERENCES

1. BLOOMGREN, J. C. Ann Surg. 60, 44, 1915.
2. GUNDEL, PAUL. Personal communication, 9 April 1942.
3. HALL, G. L. Ann Surg. 62, 15, 1915-16.
4. LOCKHART-McCORMERY, J. P. Surg. Gyn. Obst. 24, 247-250.
5. Idem. Proc. Mayo Clin. 18, 3, 439-443.
6. MINTHROP, D. Northwest M. 94, 40, 39-44.
7. RABIER, J. W. Surg. Gyn. Obst. 91, 9, 1900.
8. STEWARD, J. A. and R. HIRSH, F. W. Arch. Surg. 60, 843-849.

# EDITORIALS

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## SURGERY Gynecology and Obstetrics

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FEBRUARY, 1943

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### GEORGE CRILE

THE Editors of SURGERY, GYNECOLOGY AND OBSTETRICS announce with sorrow the death of Dr. George Crile. Dr. Crile served for many years on the Editorial Staff of the journal. An indefatigable research worker in scientific surgery and medicine, he will long be remembered for his many contributions to the art of healing. In a subsequent number of the journal more adequate recognition of his achievements will be presented.

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### THE LOCAL AND INTRAPERITONEAL USE OF SULFONAMIDE COMPOUNDS

AMPLE experimental and clinical evidence is available to establish the fact that the local use of sulfonamide preparations is an exceedingly valuable procedure in the prophylaxis and treatment of wounds sustained in civil life. Certainly, the

evidence now at hand is substantial enough to justify the continued local use of these compounds under civil conditions. It would appear, moreover, that use of these preparations in treatment of wounds inflicted under conditions of war must be considered worth while until ample evidence to the contrary is available. The final assessment of the value of sulfonamides used locally must be obtained from accurate statistical analysis of a very large group of comparable wound infections.

Perhaps the greatest difficulty encountered in such a study would be the selection of a control. To find a dependable, untreated control series of war wounds under present conditions would be difficult. At present, sulfonamides are used almost routinely in treatment of wounds of any severity sustained in warfare, probably only insignificant wounds remain untreated with sulfonamides. Since some of the severe wounds become infected in spite of the use of sulfonamides and most of the insignificant wounds remain uninfected under ordinary antiseptic treatment, the conclusion might be drawn that the incidence of infection in war wounds is higher if sulfonamides are used than if ordinary antiseptic treatment is employed. Such a conclusion probably would be erroneous.

Therefore, it appears that the best evaluation of sulfonamide compounds, as used in treatment of war wounds, would be derived from comparing the rate of infection in wounds sustained under present conditions, wherein sulfonamides are used almost routinely, as has been said, with the rate of infection in wounds sustained in the war of 1914-1918, when sulfonamides were not available. The rate of infection in wounds studied by

bacterial culture at casualty clearing stations in the war of 1914-1918 was, according to available data 73 per cent or more. For example Stokes and Tytler of the British Army obtained 310 cultures of aerobic bacteria out of 365 specimens taken an infection rate of 85 per cent. In their series all attempts at culture were made within twelve hours after infliction of the initial wound. Certainly it is difficult to conceive of infection rates this high with the present use of sulfonamides. In recent reports<sup>2</sup> of experiences in warfare for example that of Long and Ravdin the "incalculable value of sulfonamide therapy in the care of casualties" is especially mentioned.

The question of the drug of choice and its method of administration in lacerations and wounds may not yet be settled. Of the many compounds available the choice for local use probably should rest among sulfanilamide, sulfadiazine and sulfathiazole. Little difficulty has been experienced following the local use of powdered or crystalline sulfanilamide. Some of the difficulties with sulfathiazole may easily be due to the rather large amounts of material used and to the fact that it has not been dispersed evenly over infected surfaces. If finely powdered or crystalline sulfathiazole is dispersed as a thin coating rather than being "packed" in these wounds much of the irritation and foreign body type of reaction can be avoided. Sulfathiazole from the point of view of its antibacterial activity is polivalent and is not a local irritant. If the mechanical problems involved in its application can be overcome it is obviously superior to the monovalent compound sulfanilamide. Sulfadiazine may closely compare with sulfathiazole. The report of Green and Parkin<sup>3</sup> in a recent number of the *Lancet*

seems to confirm the belief that sulfathiazole is the superior drug.

The "antisulfonamide" action of pus or tissue exudate may easily be overcome by frequent cleansing of infected surfaces, followed by reapplication of the powdered drug. This is essential in the early stages of infection. Other minor objections to the local use of sulfonamides, such as absorption into the general circulation, local damage to tissue and the development of resistant strains of bacteria are easily discountable on the basis of excellent experimental and clinical experience. Further it is not necessary that the local agent penetrate deeply into the wound. The actual culture medium for bacteria is the necrotic tissue and exudate. The deeper tissues possess an adequate capacity for combating infection. The additional use of sulfonamides administered other than locally requires more diligent observation of the patient. In combat zones this may be impracticable but is of course a necessity in the presence of generalized infection. The frequent cleansing of wounds, with reapplication of finely dispersed sulfathiazole does not however require skilled supervision and is entirely feasible.

There is one field in which these compounds have without question established themselves permanently in prophylaxis and treatment, namely in intraperitoneal infection or exudation. Practically all of the objections which have been raised against the intraperitoneal use of sulfanilamide or sulfathiazole can be refuted on the basis of clinical and experimental facts. Five to ten grams of the sterile powdered drug should be introduced routinely into the peritoneal cavity in the presence of suppurative disease. Evidence accumulating that prophylactically likewise this measure is sufficiently indicated. Such prophylaxis should be especially applicable under conditions of combat wherein surgery

<sup>2</sup>Brit. J. Surg. 1943-1944. 32-34.  
<sup>3</sup>Lancet, 1944. 70.

procedures on the abdomen are likely to be complicated by infection. In selection of a drug for intraperitoneal prophylaxis the following well defined criteria should be applied (1) The drug should be active against a variety of micro-organisms, (2) it should, if possible, stimulate the local peritoneal defense mechanism and, at the same time, be innocuous to the peritoneum, (3) it should remain in fairly high concentration in the peritoneal space as long as possible, thus exerting prolonged bacteriostatic action.

Sulfapyridine and, to a lesser degree, sulfadiazine are definite peritoneal irritants and should not be employed for this type of therapy. Sulfanilamide meets some of the criteria postulated above. It is not a peritoneal irritant and does not depress the local peritoneal defense mechanisms. On the other hand, it remains in the peritoneal fluid for only twenty-four hours or even less. It is monovalent rather than polyvalent. Sulfathiazole is polyvalent. The material does not entirely leave the peritoneal fluid for a period as long as four or five days. Concentrations in the peritoneal fluid of 400 or 500 milligrams per 100 cubic centimeters are present following instillation of 5 to 10 grams. Cellular elements, particularly the mononuclear phagocytes, are markedly stimulated. There is no evidence of peritoneal irritation. Abdominal cavities opened subsequent to use of sulfathiazole have not revealed evidence of abnormal adhesions or other untoward effects.

It is not necessary to supplement the peritoneal administration of these drugs by oral or parenteral administration during the period when the peritoneal concentrations are high. The only exception to this would be the presence of some complicating disease or suppuration outside of the peritoneal cavity. Additional oral or parenteral therapy, under

ordinary circumstances, will not alter the concentrations to any significant degree but may increase the hazard of toxic reactions. In the case of sulfathiazole, further treatment is not necessary for at least three or four days. Hepatic injury rarely, if ever, occurs if the proper interval is observed between the intraperitoneal implantation and the beginning of additional therapy. Hazards of renal injury are minimal and almost insignificant if urinary output is maintained at 1500 cubic centimeters or more.

Investigators in general have experienced significant reductions in rates of morbidity and mortality following intraperitoneal use of these compounds in the presence of suppurative abdominal disease. Mortality rates for abscess and rupture of the appendix in one surgical center were more than halved in the first year of its use. Peritonitis is not commonly observed at necropsy since the introduction of intraperitoneal chemotherapy.

In view of what has just been related, it is believed that nothing should be allowed to interfere with use of one of the sulfonamides, preferably sulfathiazole, intraperitoneally in the management of infections which may occur under military conditions. Sterile packages of these compounds, weighing 5 grams each, should be part of every set of surgical supplies. Unsterilized powder can be used safely following subjection of the material to dry heat at 140 degrees C for one hour. Moist heat is undesirable in preparing the material.

Local or intraperitoneal chemotherapy obviously does not displace accepted rational supportive and surgical procedures. All of the procedures are complementary. Disagreements and clinical contradictions are products of misunderstanding of the principles concerned in the successful application of all available methods of attacking wound infections.

WALLACE E. HERRELL

## RELATIONSHIP BETWEEN THE THYMUS AND MYASTHENIA GRAVIS

EVIDENCE of an association between myasthenia gravis and abnormalities of the thymus has been accumulating since 1901 when Wegert reported finding a tumor of the thymus in postmortem examination of a patient who had died with myasthenia gravis. By 1917 Bell was able to collect reports of 56 cases of myasthenia gravis in which the thymus had been examined at necropsy and noted that tumors of the thymus were found in 10 cases and thymic enlargement or persistence was found in 17 additional cases. In 1935 Norris added a number of cases to this series and in his remarks stated that pathologic changes of the thymus may be found in cases of myasthenia gravis in direct ratio to the care with which they are sought. Blalock and his associates in 1939 and again in 1941 brought the evidence up to date by collecting data on cases from the literature and from their own experience to compile a total of 129 instances of myasthenia gravis in which the thymus was examined at necropsy or operation. They found that thymic lesions in the form of persistence, enlargement, or tumor of the thymus were observed in 71 instances, or 55 per cent of cases. In a recent publication Poer has noted that "during the last five years over two-thirds of the reported cases of myasthenia gravis in which the thymus was examined at autopsy or operation were found to have definite pathologic changes in the thymus."

At the Mayo Clinic, in the past year 7 patients having myasthenia gravis were found to have roentgenographic evidence of intrathoracic tumors. In 3 instances, surgical removal and histological study verified the clinical opinion that the tumors were of thymic origin.

Throughout the preceding years when intrathoracic tumors were searched for less diligently or rarely were intrathoracic tumors detected in myasthenic patients. Thus, it seems the Norris statement that the detection of thymic abnormalities varies with the care with which they are sought is applicable to clinical medicine as well as to pathology.

It must be admitted that the exact nature of the relationship here is not known at the present time. However the association occurs too frequently to be considered accidental. There is some evidence to suggest the myasthenia gravis may be an endocrine type of disease due to an abnormal secretion from the thymus having a curare-like effect. The thymus has often been considered to belong to the endocrine system, however no definite function of the organ has ever been proved. According to most observers, extirpation of the thymus in the experimental animal does not produce any detectable alterations, and no secretion from the gland has ever been isolated. However Adler recently has made studies which, if they can be confirmed, will be a very valuable contribution to our knowledge of the thymus and myasthenia gravis and definitely establish the thymus as a member of the endocrine system. He reported that the transplantation of thymus of puppies and calves to mature dogs and injection of extract of calves' thymus into dogs produced symptoms similar to those of myasthenia gravis and resulted in the myasthenic reaction to fasciculation characteristic of the disease. He also reported that prostigmine relieved the weakness of the dogs just as it does that of patients having myasthenia gravis. This work has not been confirmed.

Further evidence that the thymus may be a part of the endocrine system is contributed by the fact that in thyrotoxicosis and in Addison's disease the thymus is enlarged and that



in cases of myasthenia gravis have not been remarkable. This should not however lead one to disregard the evidence indicating an association between the thymus and myasthenia gravis. The subject warrants further study particularly in the fields of experimental endocrinology, pathology, and muscle physiology. We believe that in all cases of myasthenia gravis, the patient should be carefully examined for evidence of thymic abnormality and in this regard lateral roentgenograms of the chest and in some cases roentgenoscopy are extremely valuable. Naturally in dealing

with a disease characterized by remissions and exacerbations, as myasthenia gravis is, we are reluctant to state that patients have been definitely cured by removal of thymic tumors. However, we are justified in advising operation in selected cases of myasthenia gravis with tumors because patients have apparently been cured by removal of thymic tumors, because there are no other tumors, and because continued studies in this group of cases will contribute significantly to our knowledge of the relationship between the thymus and myasthenia gravis.

O. THORSON CLARK

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

THE second edition<sup>1</sup> of this very excellent review of the treatment of war wounds and the wounded represents, as Hamilton Bailey says in the preface to the first edition, British surgery. The list of distinguished authors attests to the character of the work and the solid foundation upon which it is based. That such a task could be accomplished in the midst of a great war effort is an achievement which deserves very high praise.

There is considerable rearrangement of material as compared with the earlier edition, many colored illustrations have been added, and a number of new chapters have been included. Material included in the appendix of Volume II of the first edition is brought into its proper place, sometimes by the addition of new chapters. The discussion of blast, for example, becomes a part of Chapter 4, Volume I, on compression phenomena. A brief page on frostbite and trench foot becomes Chapter 51 of 17 pages in Volume II. A new appendix is added to Volume II which represents an effort to include the most recent contributions to surgical literature.

Sections on blood substitutes and transfusion, wounds of blood vessels and burns—among others—have been considerably enlarged. Although it is stated in the section on burns that sepsis must be eliminated from the onset one would wish that the simple expedient of mask for patient and first aid workers had been mentioned as essential in achieving that objective.

The task of preparing a new edition of these volumes on war surgery has undoubtedly been achieved under great difficulties and great pressure. We have only admiration for their general excellence and the serious effort they represent. They will be of unquestioned value to the surgeon faced with the problem of treating the wounded. SUMNER L. KOCH

IN the third edition of the 600 odd page book *Disability Evaluation*<sup>2</sup> by McBride the author, a pioneer in the field of industrial surgery, has enlarged and modernized most of the sections of the book. Added is a composite schedule of approximate evaluations for partial permanent disability which is very useful for reference in determining percentage loss in a given case.

The major portion of the book is devoted to ankylosis and fracture. Since these lesions occupy a large share of industrial work, such stress is probably well placed. Chapters on hernia and head injuries are

brief, and the discussion of treatment in these sections should not be taken as a guide in their handling. An omission of importance is the failure to mention that careful cleansing and primary closure of compound wounds are desirable in favorable cases, particularly since these are more often seen in well controlled industrial cases than in any other group.

Used by many industrial commissions as a guide, this book is a necessity for the surgeon who must estimate disability in industrial cases.

THOMAS C. DOUGLASS

INJURIES to the urinary organs occur in 15 per cent of all penetrating wounds of the abdomen and frequently accompany wounds of the buttock, perineum, and thigh. Yet this important subject has received but scant mention in the manuals of military surgery.

These injuries are often accompanied by associated intra-abdominal and pelvic lesions which frequently claim the spotlight. The urinary tract involvement is often overlooked or diagnosed late. Frequently it is not discovered until the abdomen is opened for the care of an intra-abdominal injury.

The early care of these patients is usually entrusted to men in the field and in evacuation hospitals who are not themselves specialists in urology and who do not have either the time or the inclination to struggle through the somewhat controversial and confusing literature on the subject. Hence these injuries have been handled poorly in the past and the mortality has been high. Nevertheless a review of the literature reveals not a few cases of patients who survived following early and adequate definitive care, even though the injury was surprisingly severe and extensive and complicated by considerable damage to other organs. Hence early and adequate care of such injuries offers a great hope of better results. The only chance of accomplishing this lies in making the front line and evacuation hospital surgeon "urinary injury conscious" and in giving him a few simple rules of thumb to start these patients along the proper path of treatment.

The standard textbooks on urology offer very little information on this important subject since the urologist in civilian practice has very little if any experience in handling such injuries. Hence there is a great need for a concise manual to guide the military surgeon in the recognition and treatment of urinary tract injuries which occur in warfare. *Urology in War*<sup>3</sup> by Charles Y. Bidgood seems to fill this

<sup>1</sup>Urology in War: Wounds and Other Emergencies of the Genitourinary Organs Surgical and Medical. By Charles Y. Bidgood Lt. Comdr (MC) U.S.N.R. Baltimore: The Williams & Wilkins Co. 1942.

<sup>2</sup>Surgery of Modern Warfare. Edited by Hamilton Bailey, F.R.C.S. Vols 1 and 2. 2d ed. Baltimore: The Williams & Wilkins Co. 1942.  
<sup>3</sup>DISABILITY EVALUATION, PRINCIPLES OF TREATMENT OF COMPARABLE INJURIES. By Earl D. McBride, B.S., M.D. F.A.C.S. 3d ed. Philadelphia, London and Montreal: J. B. Lippincott Co., 1942.



need. This small, exceedingly well written volume of only 76 pages shows the results of considerable study and condensation, and for so short a volume it is surprisingly complete. Its scope is limited mainly to acute traumatic and inflammatory lesions of the urinary tract which are apt to occur in warfare and it is intended mainly for the guidance of the surgeon in the field and on shipboard who is not himself a urologist. By confining himself only to the most essential information and through a dogmatic presentation, which in each case usually limits itself to single mode of procedure the author has succeeded in avoiding confusion and in clarifying a rather difficult subject. The reviewer wishes, however, to take issue with a few of the recommendations in the book. Among these, the administration of blood transfusion into the corpus cavernosum penis and the recommendation to dilate urethral strictures to No. 3 to 35 F with a Kollemann dilator seem rather drastic and since they are not standard procedures might better not have been included in this volume.

FARMINGTON, CONNECTICUT.

**EXHAUSTIVE** studies of the blood cells in cancer over a period of 17 years have convinced Gerner that they give more accurate results in the diagnosis of cancer than any other tests. His routine examination of the blood consists in (1) a study of living blood by using lowered condenser crossed Nicol prisms, and dark ground illumination and (2) a study of stained blood films in respect to red blood cells, leucocytes, and platelets. In a résumé he states that cancer is most certainly not present if there is well marked rouleau formation in the fresh blood preparation, if the blood spreads easily between slide and coverglass, if there is little granular matter between the red cells, if fibrin threads do not appear within 3 minutes, if the monocyte count is under 4 per cent and the lymphocyte count over 30 per cent, if the neutrophil nuclei show smooth or regular contour. If the neutrophil count is over 80 per cent, and if there are no abnormal monocytes. In favor of cancer are viscid blood, absence of rouleaux, tight cohesion of red cells, early appearance of a dense fibrin network with abundance of granular matter in the meshes and actively moving leucocytes at room temperature, and tendency of the red cells in the centers of the "islands" or bands to undergo hemolysis, being converted into a homogeneous material. Other signs are reduction in microlymphocytes, irregular nuclear contours of the neutrophils often associated with thick nuclei, polymorphous and very large platelets, abnormality in the contour of the nucleus in the monocytes, and the occurrence of mitochondrial inclusions in the mononuclear leucocytes. All gradations exist between a definite cancer reaction and definitely noncancerous blood. Vivid illustrations are given of the diagnostic criteria and tables summarize the test results.

These studies open up a new approach in the study of the blood in cancer. More work must be done before these special tests are established as a part of the diagnosis of malignant disease.

BIRMINGHAM, ALA.

**THE** experience of one of the leading orthopedic surgeons of England, who is well known for his book *Pathologic Atlas of Chronic Arthritis (The Hand)* is presented in *Adolescent Spondylitis or Ankylosing Spondylitis* by S. Gilbert Scott. Scott describes a patient who if taken in time can be saved but if neglected either through misdiagnosis, ignorance, delay will become what he calls a "spinal wreck," which is illustrated in the illustrations.

The primary object of all medical research must be the prevention rather than the cure of disease. Prevention is not possible the next best thing is early diagnosis and complete arrest of the pathological process. The clinical diagnosis of spondylitis can be made 5 years before the onset of spinal rigidity which can be completely arrested by the use of roentgen therapy during the pre-spondylitic stage.

Spondylitis deformans includes any type of spondylitis that leads eventually to deformity. There are the spondylitis that attacks the young adult—known as ankylosing spondylitis, or preferably adolescent spondylitis—and the apical arthritis of the elderly patient—known as spondylitis osteoarthritis, or old man's spondylitis.

Scott suggests the term adolescent spondylitis for ankylosing spondylitis that attacks the young adult. The onset is insidious, extending over a period of 15 to 20 years before the appearance of spinal rigidity. It attacks the young, healthy athlete, usually the male. Infective changes are always present in the sacroiliac joints. During the active stages of a joint infection no pain is felt either over the sacroiliac joints or in the back. Bony ankylosis of the sacroiliac joint is nearly always complete by the time the clinical signs of spondylitis appear. The sacroiliac joints always present pathological changes.

If this disease is to be eradicated, radiologists must assist by making themselves familiar with the early changes in the sacroiliac joints associated with the pre-spondylitic phase. All physicians must be able to recognize the characteristic clinical history. The condition always begins in early adult life in spite of the fact that symptoms may sometimes be delayed until middle age. Attacks of rheumatic fever referred not to the back or sacroiliac joints, but to various parts of the body occurring in a young adult over a period of years, should suggest a radiologic scrutiny of the sacroiliac joints. The so-called adolescent kyphosis is not a pathological entity but is excessive kyphosis associated with the final stage of adolescent spondylitis.

**154. METABOLISM OF ANKYLISING SPONDYLITIS OR ANKYLISING SPONDYLITIS, THE EARLY DIAGNOSIS AND ITS TREATMENT BY X-RAY THERAPY.** By S. Gilbert Scott, M.R.C.S., L.R.C.P. (Ed.). D. M. E. (Camb.). Published under the auspices of the Royal Society of X-ray Therapy Research, Research No. 1. London: E. & S. Bury, 1931.

The onset of infection in the sacroiliac joints does not coincide with the onset of spinal symptoms of spondylitis. The painful and stiff spine, so characteristic of spondylitis described in textbooks, represents the last and not the first chapter of the disease. Over 90 per cent of the patients Scott examined had been good swimmers. The majority would say "I have had growing pains and attacks of wandering rheumatic pains ever since I was a boy." The only clinical sign present may be pain in the hip or ankle, or in any part except the back or the sacral region. Attacks of rheumatism in a growing youngster may be of more serious import than the symptoms might suggest.

The fundamental fact remains that changes of some sort can actually be detected by means of a radiographic examination several years before there is any clinical suspicion that the patient may eventually develop spondylitic symptoms. Scott finds the stereoscopic films are of no advantage and that the most reliable information is obtained from roentgenograms taken in the routine standard projections.

The author describes the advances in obtaining a complete radiographic record of sacroileitis. He is responsible for the treatment of sacroileitis which Americans call sacroiliac disease or sacroiliac arthritis. He describes the normal sacroiliac joint and illustrates it with gross anatomic specimens and roentgenograms. He describes prespondylitic symptoms and recurrent attacks of rheumatism in the young adult as wandering pains and growing pains. These patients sometimes have abdominal symptoms resembling girdle pains which have led to the erroneous diagnosis of gastric ulcer or gall-bladder disease. One unfortunate characteristic of these prespondylitic cases is that they have a definite tendency to be intermittent and may entirely disappear for a time with or without treatment. This temporary remission gives both the doctor and the patient a false sense of security.

Scott recommends wide field radiotherapy when other orthodox measures fail. The immediate results have so far been satisfactory.

There is a short chapter on the interpretation of the roentgenograms of the sacroiliac joints in the 1st, 2nd, and 3rd phases of the disease. The differential diagnosis includes tuberculous sacroileitis, tuberculous hip, tuberculous disease of the hip joint, sacroileitis associated with spondylitis, hip symptoms associated with spondylitis. He summarizes the signs of activity of the disease. There is an interesting chapter on calcification of the spinal ligaments and another on decalcification of vertebral and pelvic bones. Bacteriological research is described.

The remarkable results Scott so far has obtained with wide field roentgen-ray therapy in 300 cases of spondylitis in all stages extending over a period of 8 years justifies his conclusions that complete and permanent arrest of this disease is possible in a large majority of, if not in all, cases provided they are treated during the prespondylitic period.

PHILIP LEWIN

THE first edition of *Essentials of Pathology*<sup>1</sup> by Lawrence W. Smith and Edwin S. Gault was published in 1938, and the volume now reappears in its second revised edition.

The first thirteen chapters on general pathology, which, in the first edition, were disproportionately brief for a textbook, have been completely rewritten and expanded. The authors have utilized the prevailing opinions and left out controversial material whenever possible in an attempt to provide the student with a clear picture of the fundamental principles of pathology. When necessary, conflicting theories are briefly but adequately explained to relieve what would otherwise be an overly dogmatic viewpoint.

A well selected bibliography has been added to this edition, which, according to the authors, includes three types of references: documents of historical importance, recent monographs and reviews in which complete bibliographies of any particular subject may be found, and current papers of interest. The bibliography comprises sixteen pages at the end of the book and is indexed by chapter heads in Roman numerals, making ready reference somewhat difficult, however, it is a very valuable addition and greatly extends the scope of the book beyond the "essentials" for those who desire more detailed information on a given subject.

Two hundred and ninety-five brief case histories with autopsy findings are correlated with the textual material and the book is adequately illustrated with six hundred and seventy-nine uniformly excellent figures of gross and microscopic pathology, some of which are in colors and many of which are taken from cases discussed in the text.

The book is highly recommended, because of its practical clinical approach, both to the student of pathology and to the practitioner who desires a brief, readable, well illustrated reference book for a review of pathology.

D O. MANSHARDT

IT is stated by General J. C. Magee that, "The great burden of medical care in this war will fall on medical officers outside the highly specialized fields. It is thus essential that nearly all medical officers be familiar with principles of military surgery." To place in the hands of the medical officers in the field the most modern and concise information possible, the National Research Council is publishing a six volume series, each volume dealing with a different specialty as it is related to war surgery. The first volume of this series is entitled, *Manual of Standard Practice of Plastic and Maxillofacial Surgery*.<sup>2</sup> Its editorial board is made up of men outstanding in the field of reconstructive surgery.

<sup>1</sup>ESSENTIALS OF PATHOLOGY. By Lawrence W. Smith, M.D. and Edwin S. Gault, M.D., with a foreword by James Ewing, M.D. 2d ed. New York and London: D. Appleton Century Co. Inc., 1942.

<sup>2</sup>MANUAL OF STANDARD PRACTICE OF PLASTIC AND MAXILLOFACIAL SURGERY. Prepared and edited by the Subcommittee on Plastic and Maxillofacial Surgery, of the Committee on Surgery of the Division of Medical Sciences of the National Research Council and Representatives of the Medical Department, U.S. Army. Philadelphia and London: W. B. Saunders Co. 1942.

As stated in the title this book is a manual. It contains many condensed statements dealing bluntly with established procedures as well as with some debatable practices. For example the chapter on skin grafting opens with "Do not use isografts (another person) or xenografts (another species)." Reverdin (pluch) Grafts. These grafts have no place in the surgery of the face and neck. In fact they no longer have any proper place in modern surgery. And so a subject discussed at length by most others, is disposed of in a few words. Rightfully dogmatic statements are also made when it is stated, "Do not use homologous or heterogenous bone" but both "togenous (same person) and homologous (same species) cartilage is usable." As directed by this manual then, only a tografts are usable, the one exception being homografts of cartilage. It is unfortunate for many that such rules were not promulgated long ago.

First aid and emergency treatment is stressed throughout the text with due consideration being given to the question of shock in all cases. Many ingenious methods of fixing, bandaging, and transporting injured persons are described and particular emphasis is placed upon utilization of materials at hand, an important consideration when dealing with war time injuries.

The book has no bibliography but proper credit is given for the many excellent illustrations. As in all compilations of this nature, an adequate index is supplied to aid in narrowing specific points in hurry. This manual tells how and when the most effective procedure should be carried out, making a point to avoid consideration of debatable issues. It

is written to fulfill the demands of medical engaged in total war. WAYNE R. BARNETT

THE authors of *Diseases and Injuries of the Larynx* D. Chevalier Jackson and his son, D. Chevalier L. Jackson, need no introduction to the medical profession.

This remarkable book is a new edition dealing definitely clinical aspects and facts of all known laryngeal diseases. Each one is carefully considered, the definition, incidence, etiology, pathology, symptoms, diagnosis, treatment, and prognosis.

In discussing the treatment of the various laryngeal disorders great care is taken in pointing out the things which should not be done as well as those that should be done. The authors recommend that all otolaryngologists and their assistants should have a pocket infant size bronchoscope and then on the first many a newborn.

The several hundred illustrations consist of pencil, wash drawings, color plates, and letters drawn from life by the authors. Such illustrations add greatly to the teaching value of this text.

The authors in bringing this book to a new edition have added a new chapter on war injuries to the larynx. The cause and treatment of these traumatic lesions are described in detail.

The thoroughness and precision with which this book is written make it an indispensable text for the laryngologist, the general practitioner, the expert, and the student. L. F. McNIC

Illustrated by drawings of the authors. Textures of bones and fractures by Chevalier Jackson, D. M.D., F.A.C.S. and Chevalier L. Jackson, D. M.D., M.B. (Ed.) New York: The Macmillan Co. 1914.

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

STOMACH OF TUBERCULAR LESIONS OF THE FACE. By Douglas B. Parker M.D. D.D.S. St. Louis. C. V. Mosby Co. 942.

TRACTIONS. By Paul B. Magnuson, M.D. F.A.C.S. 4th ed. Philadelphia, Montreal, and London. J. B. Lippincott Co. 943.

REFRIGERATE. A NEW HYPOTHERMIA. By G. W. Theobald, M.D. (Cantab.) M.R.C.P. (Lond.), F.R.C.S. (Edin.) Colombo, Ceylon. Times of Ceylon Co. Ltd. 944.

THE HOSPITAL CARE OF THE SURGICAL PATIENT. A SURGEON'S HANDBOOK. By George Crile, J. M.D. and Franklin L. Shively, J. M.D., with foreword by E. A. Graham, M.D. Springfield, Ill. and Baltimore, Md. Charles C. Thomas, 945.

THE 946 A. A. BOOK OF VASCULAR AND OUTSTANDING SURGERY. Edited by Charles F. Panther M.D. Chicago. The Year Book Publishers, 947.

BROCHURES AND MONOGRAPHS. By Joseph Needham, F.R.S. New York. The Macmillan Co. 948.

RECENT ADVANCES IN ADRENALIN AND ASSURED (INCLUDING OXYGEN THERAPY). By C. Langer, M.D., B.S. (Lond.) D.A. (R.C.P. & S. Eng.) 949 Philadelphia. P. Blakiston's Son & Co., 950.

AMPUTATIONS OF ARTIFICIAL LIMBS. By R. D. Lee, M.D., F.R.C.S. General Editor The Rt. Hon. Lord Horder G.C.V.O. London. Humphrey Milford (Oxford University Press), 942.

THE TREATMENT OF SHOCK. By R. W. Evans (Oxon.) M.R.C.S. General Editor The Rt. Hon. Lord Horder G.C.V.O. London. Humphrey Milford (Oxford University Press), 942.

TROPICAL AND SUB-TROPICAL DISEASES. By C. B. Harber, D.S.O., M.A., D.M. (Oxon.) M.R.C.S. General Editor The Rt. Hon. Lord Horder G.C.V.O. London. Humphrey Milford (Oxford University Press), 942.

THE SEXUAL GLANDS OF THE MALE. By Oswald S. Lowney, A.B., M.D. F.A.C.S. Collaborator Frank R. Lowney, A.B. M.D. F.A.C.S., and Donald R. Smith, A.B. M.D. F.A.C.S. (Reprinted from Oxford University Press, New York, London Toronto Oxford 1914).

# SURGERY

## GYNECOLOGY AND OBSTETRICS

*An International Magazine, Published Monthly*

VOLUME 76

MARCH, 1943

NUMBER 3

### MULTIPLE GASTRIC POLYPOSIS

A Supplementary Report of 41 Cases, Including 3 New Personal Cases

FELIX L. PEARL, M D, and HAROLD BRUNN, M D, F A C S, San Francisco, California

IN 1926, Brunn and Pearl (13), stimulated by the occurrence of successive cases, reviewed the subject of multiple polyps of the stomach, and collected from the available literature 78 cases having 3 or more polyps. To this they added 6 proved cases of their own and reported 7 probable cases, giving a statistical analysis from the more important viewpoints. In addition, they discussed at some length the incidence, diagnosis, symptoms, signs, pathology, and treatment of the disorder, which the reader may consult for details.

In that communication stress was laid on the elusiveness of gastric polyposis to the diagnostician, and a case was reported in which, despite their awareness resulting from intimate contact with literature and cases, the authors made an incorrect preoperative diagnosis. This case displayed a suggestive history, the usual laboratory findings of anacidity and bleeding, and the characteristic roentgenological picture (Fig 1) of multiple gastric polyposis, but at operation was found a marked hypertrophic gastritis without polyps (Figs 2, 3, 4). It is more probable that a correct diagnosis would have been made had gastroscopy been utilized in the investigation.

In that article they also called particular attention to the difficulties in pathological diagnosis and classification of these growths, and to the incidence of malignant alteration of 12 per cent.

Notwithstanding our interest, 2 more cases of multiple gastric polyposis came to autopsy having eluded antemortem diagnosis, one of them (Case II)<sup>1</sup> even after a competent roentgenological examination. In addition, once again, as in our previous series, the diagnosis of multiple polypoid growths of the stomach was made in error on the basis of clinical, roentgenological, and laboratory evidence, but the stomach resected by one of us (H B) showed a marked hypertrophic gastritis (Case IV).

These misadventures aroused us to reconsider the entire subject of multiple gastric polyposis and induced one of us (F L P) to collect from the literature all the additional cases of 3 or more gastric polyps reported since our previous compilation, appending the reports of our 3 recent cases (Table III). The data from these 41 cases will be presented as a separate series and the statistics compared, when indicated, with those of our previous inventory of 84 cases. Since the recent reports

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<sup>1</sup>Roman numerals refer to cases reported in text. Arabic to collected cases in Table III.

are much more complete than the early ones, their collected series will be far more trustworthy than the former group for statistical deduction.

#### INCIDENCE

Multiple gastric polyposis is not common. Previous data on incidence however are not reliable. Many cases are undoubtedly overlooked because of lack of symptoms. The authors were previously able to collect only 79 cases from 1820 to 1926 adding 5 of their own. From 1926 to 1941 however they found 38 reported cases adding 3 of their own. This increase in incidence may be only apparent, reflecting a greater acumen in diagnosis and a willingness to report rather than a true increase in frequency of the disease. Thirty of the 41 cases occurred in males. The youngest was 23 the oldest 80. Two-thirds of the cases were discovered in the 4th and 5th decades. This gives no information as to how long the condition was present inasmuch as it may lie dormant for an indeterminate period.

#### ETIOLOGY

There are two recognized theories regarding the origin of multiple polyps of the stomach. One group including Wechselmann and Rippert is of the opinion that they are of congenital origin—true neoplastic growths. The occurrence of the disorder in twins in 3, 4 and 6 siblings, in a mother and son seems to support this contention. In our combined series of 125 cases, however we have not found a single instance in which a familial predisposition was evident. It is otherwise with certain strains of mice. Stewart (105) reported the occurrence in the pyloric chamber of almost all his strain I mice of both sexes diffuse lesions characterized by adenomatous, hypertrophic and hyperplastic overgrowth of glandular rugae. This is definitely inherited as a recessive character. The absence of well marked hereditary tendencies in our human cases and the almost universal appearance of hereditary adenomatous growths in these mice cannot now be correlated. Noteworthy is the difference between multiple gastric polyposis in which hereditary influence is questionable and between colonic

polyps in which hereditary factors are strong.

A second group, among which are Cohn (23-24) Menetrier (68-69) and Verne (27) that the growths are due to chronic inflammation. Konjetzny claims to have found 2 stages in the chain from hypertrophic gastritis to adenoma, and finally to carcinoma. Adenopapillomas have been produced by chronic irritation resulting from the use of nematodes and by other methods.

The relationship between gastritis, adenoma, and carcinoma, is now receiving considerable attention from the profession. The high incidence of achlorhydria in our series of cases of multiple polyposis indicated that the condition is associated with widespread changes in the function of the gastric epithelium. Similar types of gastric reactions are found in over 60 per cent of cases of carcinoma. In 36 cases of multiple and single adenomas observed by Schindler through the gastroscope in 2167 patients, 26 had a definite gastritis of this number 20 were atrophic, 2 superficial and 4 hypertrophic in type. Conversely 83 per cent of 1,814 patients without atrophic gastritis had visible adenomas whereas 6 per cent of 353 patients with atrophic gastritis had adenomas.

Inasmuch as patients with pernicious anemia regularly also have gastric achlorhydria, studies have been made to determine a possible relationship between pernicious anemia and multiple adenomas. Schindler found gastric adenomas in 6 of 43 patients suffering from pernicious anemia but did not mention whether they were single or multiple. There is a much greater incidence than that found in patients not having pernicious anemia. Rhodes notes that gastric polyposis is more common in cases dead of pernicious anemia than in those dead of other causes. Maklaine Brown (112) in a study of the stomachs at postmortem examination of patients dead of pernicious anemia found chronic gastritis regularly present. She also noted that the incidence of benign gastric tumors in 19 autopsies on patients dead of pernicious anemia was 8 per cent whereas the incidence in 18,200 autopsies of patients without pernicious anemia was only 0.003 per cent.



TABLE I—SYMPTOMS AND PHYSICAL SIGNS—  
41 CASES

	No. cases percent
Pain or distress	3
Anorexia	8
Nausea	4
Vomiting	5
Diarrhea	7
Hematemesis	4
Weakness	6
Constipation	7
Tumor	9
Tenderness	
Rigidity	

Perforated duodenal ulcer

considerable variation from the normal. Many are elongated tortuous, and dilated some have been changed into small cysts containing old secretory material. At times the epithelial lining shows proliferation in the form of atypical papillae. Superficial ulceration and necrosis with inflammatory infiltration often occur. The epithelial cells may be of the undifferentiated tall, hyperchromatic type or of the type resembling the cells of the large intestine. There may be mixtures of goblet cells, Paneth cells, and the fuchsinophil cells of Lubarsch with transitions from one to another even in the same gland.

The *hyperplastic polyps* show a microscopic picture usually easily differentiated from the true fibroadenomas. The muscularis mucosae is always intact and the submucosa makes no attempt to insinuate itself into the hyperplastic area to form a core. The enlargement which forms the polyp is composed of a purely mucosal proliferation in which the epithelial and fibrous components both play a part. The glands become hypertrophied, deeper, larger, and heavier and the fibrous tissue becomes increased, but there is no irregularity in the fundamental character of the glandular and fibrous components or in their interrelationships. The undifferentiated hyperchromatic cell is rarely seen. The epithelial cells may resemble those of the normal stomach for that area, or they may be replaced by the colonic type of cell. Cystic dilatation is less common. These hyperplastic areas are not sharply delineated but merge imperceptibly into the adjacent mucosa. Inflammatory cells are generously disbursed throughout the hyperplastic area and the mucosa adjoining it.

In some cases both neoplastic and hyperplastic types may appear in the same specimen. At times the microscope just may not fit readily into the classification given making it difficult or even impossible to place the abnormality in a clear-cut neoplastic or hyperplastic category.

Interesting is the fact that the condition of multiple gastric polyposis stops abruptly at the duodenum. In Case 31 duodenal involvement was diagnosed roentgenologically at an operation, but it is more probable that the surgeon felt gastric polyps prolapsed into the duodenum. Since no specimen was available, the proof of duodenal participation was lacking. We know of no case in which the condition was proved to include the duodenum.

#### SYMPTOMS AND SIGNS

There are no symptoms which are characteristic of this disorder. Epigastric pain or distress was the most frequent symptom, but present in 31 cases of this series. Hematemesis was present in 7. In 2 cases (Cases 1 and 2) it was the presenting symptom. In 1 (Case 11) it caused death. Evidence of bleeding gross or occult was found in the stools in 14 additional cases. In 5 cases gross bleeding was evident on examination of the stool. Thus bleeding is known to be present in 21 of the 40 cases. Diarrhea was noted in 5. It is probably the result of the achlorhydria which is such a common finding. In 2 cases it was the presenting symptom. For 25 years one patient (Case 2) suffered from diarrhea which disappeared promptly following excision of the polyps. The frequent complaint of weakness (14 cases) is probably due to bleeding from ulcerated polyps. Fourteen complained of vomiting. The incidence of symptoms is indicated in Table I.

Pedunculated tumors are more apt to give symptoms than broad based ones. Tumors on a long thin stalk may become detached, appearing in the vomitus (Case 31), in the gastric lavage water, or attached to a stomach tube used for diagnosis or treatment (13, 20, 118) or they may be found in the stool (118). Indeed the first antemortem diagnosis was made at operation in 1909 because of a piece of tumor tissue found attached to the stomach tube (118). The separation of polyps from

cause pain and bleeding. Tumors near the pylorus are more likely to cause spastic symptoms, one or a group of freely movable polyps may prolapse through the pylorus into the duodenum, thus producing partial or complete pyloric obstruction (13, 23, 25, 78) as in Cases 7, 16, 20, 33.

Some patients have had symptoms referable to the stomach for many years. Durations of 20 years or longer have been reported by Wegele—29 years, Menetrier (68)—25 years, Brunn and Pearl (13)—25 and 20 years, several others have had symptoms lasting over 10 years. Diarrhea was the only symptom in Case 2 for 25 years, it disappeared promptly after excision of the polyps. Sudden increases in severity of symptoms should warn one of the possible onset of malignant degeneration as in the case reported by Brunn and Pearl. Long remissions may occur.

In 7 cases a tumor mass was palpable. In our previous report, a palpable mass was noted in only 1 case. Tenderness was present in 9 cases. Rigidity was found in only 1 case, this being due to the associated perforation of a duodenal ulcer (Table I).

#### DIAGNOSIS

It is not surprising that a disease which may remain symptomless for so long should be so difficult to detect during life. At the time of our last report (13) we believed that the x-ray picture was so characteristic that the diagnosis could be made in the great majority of cases by roentgenography, it was then that we improperly diagnosed a case of hypertrophic gastritis as diffuse gastric polyposis (Figs 1 to 4). It is clear from our experience that one cannot rely on the x-ray to make the differential diagnosis between multiple gastric polyps and hypertrophic gastritis. Food particles in the stomach, bezoars, and sarcoma may also be difficult to differentiate roentgenologically. In our recent series of 41 personal and collected cases, the correct diagnosis was made by x-ray in 17, by operation in 13, by examination of the excised surgical specimen in 5, and by autopsy in 6.

We have analyzed our series from the roentgenological standpoint, comparing the roentgenological diagnosis with the findings at

operation or autopsy. It is somewhat difficult to evaluate the status of the x-ray in the diagnosis. Roentgenological reports are available in 36 cases. In 5 of these the main x-ray diagnosis was obviously incorrect. In the remaining 31 the main roentgenological diagnosis was correct as far as the essential lesion was concerned, but in 14 instances polyps were completely overlooked. For example in our Case II the roentgenologist diagnosed a diaphragmatic hernia, but overlooked typical filling defects of gastric polyps in the herniated cardia which were evident on retrospect examination of the films. In 11 instances the type of lesion was correctly diagnosed but the number of lesions reported by the roentgenologist was less than that found in the specimen. In 8 instances, the diagnosis was correct in type, but involved areas were missed. Lesions of the cardia more easily escape notice because pressure on the barium shadow is difficult. Occasionally the roentgenologist diagnoses polypoid tumors when only a marked hypertrophic gastritis exists. This occurred in a case report of Brunn and Pearl (13), and in Case IV. One must take into consideration that the cases in this series were collected from widely separated sources, and that the individual experience of reporting authors in this uncommon affection is not great.

Although the first case of gastric polyposis diagnosed by gastroscopy was reported in 1922 by Schindler (99), it is only recently that this method of diagnosis has come into more general use. The more frequent employment of gastroscopy in vague gastric disorders will undoubtedly increase the number of cases diagnosed during life. The gastroscope is particularly valuable in diagnosing mucosal lesions, and was responsible for the visualization by Dr Allan Cohn of gastric polyps in our Case III, in which the roentgenologist interpreted the x-ray filling defects as due to retained food. There need be no rivalry between the 2 methods, each is complementary to the other, each has its limitations, and neither should be used to the exclusion of the other. The combined use of roentgenography and gastroscopy in the diagnosis of obscure gastric complaints will afford us more accurate diagnosis than we have ever known before.



TABLE II.—LABORATORY DATA

	Total cases	% cases
Gastric analyses		
No free hydrochloric acid	24	
Blood	3	5
Tumor tissue	5	
Myorrhea	3	4
Occult blood—stool		6
Anemia		5
Blood Wassermann—negative		

The diagnosis of malignant degeneration of gastric polyps in the living subject is still an unsolved problem. The pathologist himself may be unable to settle this important question in the excised stomach and in the microscopic preparations made therefrom. Unfortunately the stomach cells change very quickly after the blood supply has been arrested, thus confusing the microscopic picture. Too pathologists often disagree as to the criteria of malignant alteration. Therefore it is much to expect of the roentgenologist or the gastroscopist to diagnose malignant degeneration in borderline cases. Some gastroscopists claim their ability to make this differentiation by characteristics which are visible through the instrument but not apparent in the excised specimen or at autopsy. This will be a great step forward if their contention is upheld by further study. In certain cases, outspoken deep infiltration of the gastric wall is disclosed by the x ray or the gastroscope. In our present series of 41 cases, only 27 gave satisfactory

gastric secretion observed following the use of histamine. Blood was noted in our series in 5 cases. No tumor tissue was found in the gastric content but this should not deter the examiner from making careful search for small tumor particles, especially in the specimens showing blood. The discovery of polypoid tumor tissue gives indisputable evidence of the presence of such tumors but not of their malignancy. The latter condition can be judged only in specimens which contain the submucosa in which alone malignant invasion can be demonstrated. In fact Wegele made the first antemortem diagnosis at operation for a suspected carcinoma which he had erroneously diagnosed from a piece of tumor tissue expressed through the stomach tube. Thus in Case 14 malignancy could not be demonstrated in tumors removed for biopsy but was definite 4 weeks later at autopsy. The presence in the gastric content of fresh blood, associated with increased mucus is suspicious of the presence of gastric polyps. If there is also an absence of free hydrochloric acid the diagnosis is much more probable. Conversely one should hesitate to make this diagnosis in cases having considerable free hydrochloric acid in the fasting content. Bruno and Ivori (13) reported a case with known acidity for

usual measures. Severe gastric hemorrhage, the vomiting of increased quantities of mucus, or the persistence of occult bleeding in the stool without apparent cause are suggestive findings which demand a complete roentgenological and gastroscopic investigation by specially trained men.

#### TREATMENT

In the present series the surgical treatment consisted, for the most part, in (1) local excision of all polyps and (2) gastric resection. In a small number of cases resection was combined with excision of a few polyps remaining in the gastric stump. In one case (Case 38) polyps were removed by a diathermy snare through a gastrostomy (42). Medical treatment only was given in 3 cases, all of which terminated fatally, one from hematemesis (Case 1), one from alcoholism (Case 19), and 1 from streptococcus viridans septicemia (Case 22). A more detailed analysis from the standpoint of surgical treatment follows.

*Local excision of all polyps.* This procedure was carried out 8 times. Two patients died of the operation. Two were well up to 6 weeks after operation. Further details regarding the course of the individual cases are as follows.

Of the 4 benign cases, the results of local excision of the polyps were: Case 2, patient relieved (no dates), Case 10, patient died 2 days after operation from peritonitis, Case 17, patient well with a 16 pound weight increase 6 weeks after operation, Case 30, death after 1 year. Of the 4 malignant cases, the results of excision were: Case 13, patient died of pulmonary edema, 1 day after operation, Case 8, recurrence of pain, 3 months after operation, Case 21, patient was relieved for 5 years and then had an operation for recurrent polypoid tumors and died, Case 28, relief for 5 years, then recurrence of symptoms.

The short follow-up period in many of these cases makes any deductions unreliable. Of the 2 benign cases which survived the operation (Cases 2, 17) both were greatly improved, but whether malignancy supervened after the short observation period cannot be learned. The malignant cases made a poor showing. Not one had a satisfactory result. Two were relieved for 5 years (Cases 21, 28) before the

return of symptoms and signs denoting recurrence of malignancy, in one of these, an extra-gastric gland showed no microscopic evidence of malignancy 7 years before. One is struck with the inadequacy of local excision in the treatment of multiple gastric polyposis and with the danger of making any prognostication even 5 years after operation.

*Gastric resection* was carried out 19 times. In Cases 23, 24, 36, one or more polyps were excised from the gastric stump. Four patients died of the operation, one in 3 days of severe anemia, one in 12 hours of pneumonia, 1 in 2 weeks of a complicating subphrenic abscess, and 1 in 5 days of peritonitis and jaundice. Five cases gave no follow-up data. Of the remaining 10 cases, 7 patients were alive and symptomless from 6 months to 4 years after operation. One other patient (Case 9) was alive 1 year after operation with probable liver metastasis, and one (Case 4) had a blood picture resembling pernicious anemia. Of the 19 patients treated by resection in 2 cases no malignancy data are given. Of the benign cases 2 (Cases 29, 34) died of the operation, one following a complete gastrectomy. The courses of the 9 benign cases are: Case 3, patient had uneventful convalescence (no dates), Case 4, patient's blood resembled that of pernicious anemia, Case 11, no data, Case 20, complete relief (no dates), Case 23, complete relief 7 months after operation, Case 25, no data, Cases 29 and 34, patients died of operation, Case 35, patient well 15 months after operation. Of the 8 malignant cases, 2 patients died of the operation (Cases 12, 41). The disposition of the 8 malignant cases is as follows: Case 7, patient well 1 year after operation, Case 9, liver metastases 1 year after operation, Case 12, patient died of operation, Case 24, patient had complete relief (no dates), Case 33, patient well 4 years after operation, Case 26, no data, Case 37, patient well 6 months after operation, gained 10 pounds, Case 40, patient died 5 days after operation of peritonitis and jaundice. Two cases gave no malignancy data.

Thus, of those which survived gastric resection, 4 of the 5 benign cases had a satisfactory result from 1 to 4 years after operation. In comparison, a satisfactory result was obtained

in 2 of the 3 benign cases (up to only 6 weeks) and in none of the 4 malignant cases which survived local excision. The authors emphasize the inadequacy in number and follow up data of these cases, but the superiority of gastric resection as a routine method of treatment is strongly indicated. Most important is the fact that gastric resection eliminates the possibility of the onset of malignant degeneration such as occurs in the bases of excised polyps.

**Biopsy** In 6 cases (Cases 5 6 14 15 16 38) one or more polyps were removed through a gastrotomy for microscopic examination or to control bleeding. Only one of these (Case 5) had a happy result—well 3 years later. Case 15 gave no follow up data. In Case 14, patient died of bleeding 4 weeks after excision of a polyp for hemorrhage. In Case 38, 50 polyps were removed by a diathermy snare through a gastrotomy but many were left; death occurred 2 months later of general debility and liver insufficiency. Except for Case 38 no attempt was made in these to eradicate all the tumors but merely to stop bleeding or to obtain specimens for diagnosis.

It is thus apparent that the only safe method of treatment is the surgical removal of the tumor bearing area by gastric resection. The occurrence of malignant degeneration in this series in 19 of 37 cases giving malignancy data places gastric polyposis close to colonic polyposis in its tendency to malignant change and argues for wide removal. If the entire tumor bearing area cannot be amputated as much of it should be resected as possible and any tumors remaining in the stump should be excised and their bases thoroughly destroyed with cautery.

If the condition of the patient does not permit gastrectomy and if there are only a few discrete polyps, the surgeon must compromise by excising the individual tumors and thoroughly destroying their bases. If there are a large number of polyps widely distributed over the mucosa, it is futile to attempt excision of only a few except for diagnostic purposes. Bleeding should be controlled and the patient returned to bed. When he has been thoroughly prepared and his condition satisfactorily improved, a gastrectomy again should be attempted. If possible the patient

should not be subjected to surgery unless his condition warrants the performance of a partial resection. Whole blood or plasma are often useful before and after operation. Gastrostomy is of no value.

If the differentiation of multiple gastric polyps into neoplastic and hyperplastic types is valid, the incidence of malignant degeneration may differ in the two types. From the microscopic descriptions in the reported cases it is not usually possible to make this differentiation. One would expect the coexistent polyps to have a higher incidence of malignancy. For the time being each case should be conducted in accordance with the total incidence of malignant degeneration. Further studies may allow us to alter our prognosis with the determination of the type of polyps.

#### PROGNOSIS

In our previous report we found 12 per cent of cases malignant. Many of the cases in this series were reported long ago and the data were incomplete. In the present series of 41 cases 4 gave no malignancy data. Of the remaining 37, 19 were malignant. Statistics of other authors vary. Thus Lawrence found 15 per cent malignant degeneration in 50 amputated cases of gastric polyps, over half of which were multiple. Stewart (106) found 25 per cent malignant degeneration in 47 cases, 10 of which were multiple and Miller Eason, and Wright noted such changes in 20 per cent of 25 collected and personal cases.

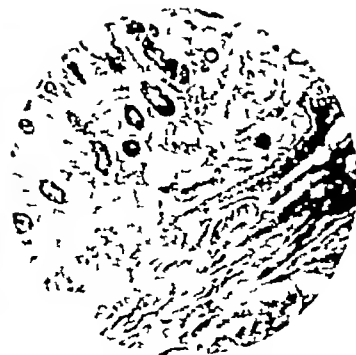
The occurrence of malignant degeneration in over half of our present series argues for prompt and radical surgical measures. Fifteen patients were dead in from 1 day to 5 years after the institution of treatment. Gastric resection offers the best outlook and will eliminate the high incidence of malignancy if all the tumors are removed with the resected portion. In some cases the disease remains benign for many years, but each case should be treated by operation as soon as the diagnosis is reached and the patient satisfactorily prepared. Procrastination is useless and harmful. If malignancy has not yet supervened, gastric resection can produce an excellent result. If malignant invasion has occurred it is the most efficient method of treatment. The



Fig 1

Fig 1 Severe hypertrophic gastritis erroneously diagnosed "diffuse polyposis." The roentgenogram is typical of polyposis but operation showed a marked hypertrophic gastritis.

Fig 2 Photomicrograph of specimen in case shown in Figure 1. Inner layer of mucous membrane: 1, General



Fig



Fig 3

edema and dilatation of capillaries, 2, extension of infiltration among fibers of edematous muscularis mucosae, 3, vessel containing large number of leucocytes.

Fig 3 From same specimen as in Figure 2. Surface of mucous membrane: 1, edematous region, 2, cellular infiltration, 3, tortuous glands.

number of patients operated upon is too small and the period of observation too short to give reliable prognosis, but the gravity of the condition as a precursor of cancer is obvious.

#### REPORT OF PERSONAL CASES

CASE I G B, a male, aged 50 years, complained of intermittent attacks of constipation, flatulence, and bloody stools, occurring every 2 or 3 months, for the past 3 years. In the past year they were more frequent and severe. He had no nausea, vomiting or abdominal pain. There was slight soreness of the abdomen. He lost 4 pounds in the past 3 months. There were no serious past illnesses. He entered the hospital for study on January 3, 1938. Proctoscopic examination showed multiple growths of the descending colon. Two biopsy specimens were diagnosed by Dr. Rusk as "mucosal hyperplasia, no evidence of malignancy." A roentgenological examination of the large bowel showed multiple polyposis of the entire colon.

Since entry he had nausea and vomiting associated with distention which did not react to conservative measures. The stomach was kept empty with suction and the return water was always clear. Because of constant vomiting and distention an ileostomy was done on January 10, 1938, by H B. Since that time he had had constant abdominal pain and vomiting. The vomitus contained gross blood. The suction was continued. On January 18, 1938, his temperature reached 39.6 degrees C, leucocytes numbered 23,600 with 97 per cent polymorphonuclears. On January 21, 1938, a considerable amount of bright red blood was evacuated from the stomach through the tube. The tube was removed. The patient made a sudden exit

At postmortem examination the following were noted. The stomach contained no blood. The cardia and upper fundal portion was studded with a large number of small, hemorrhagic polypoid growths, the largest only a few millimeters in diameter (Fig 5). The gastric mucosa was ecchymotic in this region. There was a multiple polyposis of the entire colon from the cecum to the anus. Microscopic examination

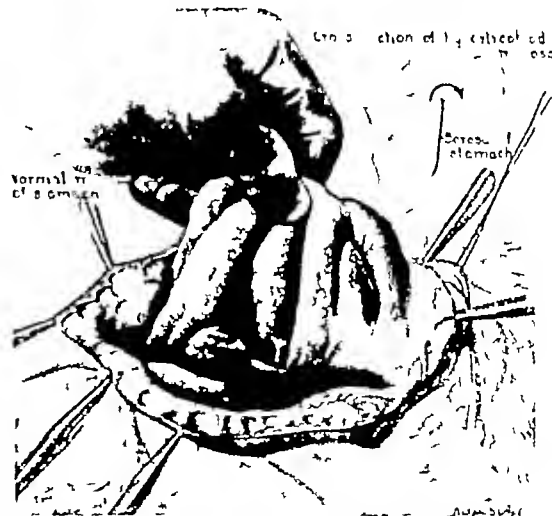


Fig 4 Same case as in Figure 1. This shows the enormously hypertrophied folds of gastric mucosa as they are actually being withdrawn from the stomach through the gastrotomy incision. An area of hemorrhage and ulceration is shown.

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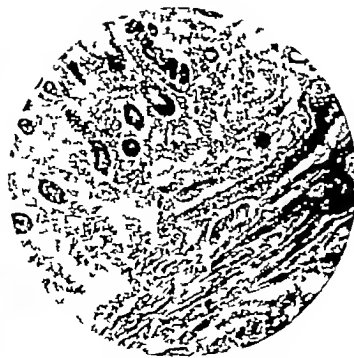


Fig 2

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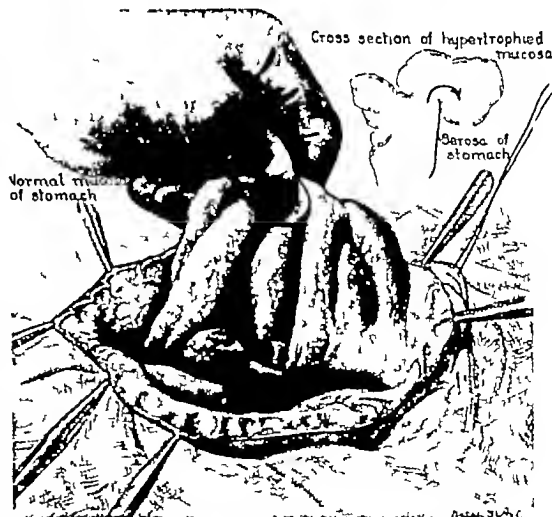


Fig 4. Same case as in Figure 1. This shows the enormously hypertrophied folds of gastric mucosa as they are actually being withdrawn from the stomach through the gastrostomy incision. An area of hemorrhage and ulceration is shown.



Fig. 5. Case I. There are numerous small polyps principally in the cardiac and fundal portions of the stomach.

tion of the stomach showed the mucosa to be drawn into many small polypoid tumors. Most of the polyps were attached to the mucosa by tiny stalks into which the muscularis mucosae, split into fine strands at the base invaginated itself while the submucosa followed into the stalk to lesser extent. Varied was the degree of participation of the muscularis mucosae, especially of the submucosa in the formation of the stalk. The submucosa sometimes merely projected itself at the base of the polyp into low gradually arising peak, with only a small amount of its connective tissue taking part in the formation of the stalk (Fig. 6) in other instances it thrust itself well into the stalk its connective tissue contributing to a greater or lesser extent to the groundwork of the tumor pattern (Fig. 7) The gastric glands in the region of the polyps showed little variation from the normal, except for some increase in the number of mucous cells. The stroma was normal except for slight edema. There was no noteworthy increase in lymphocytes or plasma cells. The gastric mucosa between the polypoid growths was normal. The colon showed the usual picture of multiple polyps with adenocarcinomatous degeneration on one polyp in the cecal region.

This patient came to autopsy without any thought in the mind of the attending physician of finding a pathological process in the stom-

ach. All of the symptoms could have been explained on the basis of colonic polyposis with obstruction. The pathological picture in the stomach conformed more to the connective tissue type, but the epithelium was not neoplastic.

**CASE II.** S. H. male 78 years of age, entered hospital April 6, 1935, complaining of pain in the chest of 3 years duration. He had had symptoms since 1932 and received adequate antileptic therapy. In January 1933 he complained of pain in the epigastrium and vomiting whenever he ingested a large meal. Roentgenological examination showed hernia of the fundus of the stomach through the diaphragm. This was held to account for his gastric symptoms.

Examination showed typical cardiac insufficiency with decompensation and marked dependent edema. Blood pressure was 90/70. Blood and spinal fluid Wassermann were negative. There was no edema. He expired suddenly.

At postmortem examination the following were noted. The mucosa of the stomach was covered by numerous polypoid masses arising from the mucosa 3 centimeters in diameter diffusely scattered, but mainly grouped along the lesser curvature of the stomach (Figs. 8 and 9). All were pedunculated and had thin stalks. Some of the polyps showed superficial necrosis. There were no polyps in the small intestine but there were 6 similar polyps in the cecum. There was no gross evidence of malignancy.

Microscopic sections of the stomach (Fig. 10) showed the polyps to be composed of tall columnar epithelium arranged in acini around central cores. Some of the acini were greatly dilated and contained faintly stained pink material. The epithelium showed some hyperplasia but the cells were not markedly altered and there was no evidence of malignant degeneration. The transition of the mucosa from the normal to that described as very gradual. At the attachments of the polyps to the mucosa the muscularis mucosae was split and its fibers carried into the stalk, often into the tumor itself. The submucosa, too, followed the muscularis mucosae, its connective tissue entering the stalk and forming part of the stroma of the tumor. Occasional lymphocytes were seen in the stalk. Sections from the colon showed a small polyp composed of rather uniform small acini lined by tall columnar epithelium but was distinctly piled up in places and contained occasional mitotic figures. The stroma was compact and had numerous lymphocytes plasma cells and eosinophiles. There was no evidence of malignancy.

The presence of gastric symptoms of 3 years duration were amply accounted for by the hernia of the fundus of the stomach through the diaphragm. From the clinical standpoint the discovery of multiple gastric



Fig 6 Case I Sections through the stomach show the small polypoid tumors arising from the mucosa. In this section the muscularis mucosae tends merely to dip into the stalk and does not enter the tumor. The submucosa plays little or no part in the formation of the polyp. The epithelium shows little variation from the normal.



Fig 7 Case I The muscularis mucosae and the submucosa enter the stalk for a greater distance than in the previous figure. Here the muscularis mucosae and the submucosa insinuate themselves into the stalk and contribute to the formation of the groundwork of the tumor.

polyposis in the autopsied stomach was a surprise. The x-ray films previously taken in 1931 were again inspected. The ectopic position of the fundus was noted, but the roentgenologist had completely overlooked filling defects characteristic of polyps in the herniated portion. The error in not discovering these lesions before death, is therefore, an oversight on the part of the roentgenologist. The case falls into the class of congenital polyps.

CASE III B S, a retired salesman of 74 years entered Mt Zion Hospital May 23, 1940. He was well until 6 weeks ago when he developed vomiting following the ingestion of solid foods. This usually occurred several hours after eating. The condition became steadily worse so that during the past 2 weeks he could only retain eggs and liquids. He regurgitated his food at night. This was never sour or bitter. The vomitus occasionally was streaked with fresh blood. He had no abdominal pain. His stools were not bloody or tarry. He had been subject to chronic constipation for years. Since the onset of his illness he lost 15 pounds in weight. He smoked moderately, used no alcohol.

On physical examination one found an avoird mass in the epigastrium about 6 centimeters in diameter, nontender, smooth, and movable. A smooth liver edge was felt 3 centimeters below the costal margin. His blood pressure was 90/60. There were no other abnormal physical findings.

Roentgenological examination May 15, 1940, at Stanford Hospital showed 90 per cent retention in 5 hours. The stomach was large, containing much fluid and particles of food material. At the pylorus was

felt a tumor which constricted the lumen considerably and left the wall stiff. Vigorous peristaltic waves ran down to this area and stopped promptly. The roentgenological diagnosis was "carcinoma of the stomach."

Gastroscopy was performed by Dr. Allan Cohn on May 29, 1940, with the following report: The entire antrum is involved in a diffuse carcinomatous nodular process with a polypoid excrescence. The body of the stomach is similarly involved by a diffuse nodular process, with a polypoid excrescence presenting from the lesser curvature. The changes extend well into the upper third of the stomach, but the tumor edge cannot be well seen because of a mucous lake.

Impression: Diffusely infiltrating carcinoma.

Laboratory investigation revealed the following positive findings: urine—albumin, very slight trace, sugar, negative, leucocytes, 3-5 per high dry field, erythrocytes—30-50 per high dry field. Blood—hemoglobin 10.8 grams, red blood cells, 4,100,000, white blood cells, 6,600, differential count, normal. Stool—occult blood moderately positive. Blood Wassermann—negative. Gastric analysis (alcohol meal) showed:

	FC	r	2
Cubic centimeter	40	80	60
Free hydrochloric acid	0	0	0
Total hydrochloric acid	10	5	5

The clinical diagnosis was carcinoma of the stomach. Operation was performed by Dr. F. I. Harris on May 31, 1940. Exploration revealed a nodular tumor occupying the pyloric end of the stomach. Several enlarged lymph nodes were felt in the lesser omentum. The liver was normal. A subtotal gastric resection of the Hoffmeister-Finsterer type was performed. The involvement of the neoplasm was so extensive that the line of resection was through the tumor and part of the growth was left *in situ*. The postoperative diagnosis was "gastric carcinoma with metastases to the lesser omentum and retroperitonea."





Fig. 8. Case II. Many pedunculated polyps are seen diffusely scattered over the gastric mucosa, but especially numerous over the mucosa of the lower third of the stomach. One hundred eleven polyps were counted. The mucosa between the tumors appears normal.

lymph nodes. The patient died on the 5th day after operation with jaundice, peritonitis, and terminal pneumonia.

In the specimen, multiple large nodes were felt through the serosa on the anterior and posterior walls; one large firm mass was felt in the antrum.



Fig. 9. Case II. A pedunculated polyp showing the muscularis mucosae and the submucosa entering the stalk and forming the groundwork of the tumor pattern. Dilated gastric glands are visible.

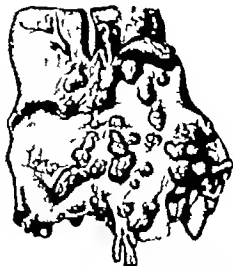


Fig. 10. Case II. The lower third of the stomach showing the polypoid growths separated by apparently normal mucosa.

When the specimen was opened a large stenosing, ulcerated carcinoma involving almost the entire antrum was found. Most of the remainder of the stomach was covered with a large number of soft polypoid excrescences, some as much as centimeter high (Fig. 11). From 3 to 6 centimeters of normal appearing mucosa separated the areas of multiple polyps from the carcinoma. The resection was through an area of multiple polyps.

Microscopic examination of the stomach (Fig. 12, 14) showed the muscularis thick and hypertrophied. In the submucosa were several focal accumulations



Fig. 11. Case II. The gastric glands are affected. The glandular epithelium shows some hyperplasia but the cells are not markedly altered.



Fig 12 Case III A large number of closely placed polyps are seen in the cardia and upper fundal portion of the gastric mucosa. In the pyloric portion is a large ulcerating carcinoma. A strip of normal appearing mucosa separates the carcinomatous area from the area bearing the polyps.

of plasma cells and lymphocytes with a few scattered polymorphonuclear leucocytes. The polyps were composed of a thick layer of rather hypertrophic gastric mucosa arranged about a central core. The cells lining the glands were tall and had an abundance of clear cytoplasm of the mucous type. They showed no striking variation from the normal. At the area of attachment of the polyp, the muscularis mucosae was split and its fibers entered the growth, its connective tissue contributing to the formation of the core. In many places the polyps branched. There was no evidence of malignant alteration. Three similar polyps were found in the colon, 1 in the bladder

The diagnosis of the clinician, the roentgenologist and the gastroscopist before operation, and the surgeon at operation was carcinoma. The specimen showed the carcinoma, but in addition a widespread multiple gastric polyposis with individual tumors projecting into the lumen as far as 2 centimeters. It is true that at gastroscopy two polypoid growths were noted by Dr. A. Cohn, but the essentially diffuse and multiple character of the benign lesion was not even then recognized. The

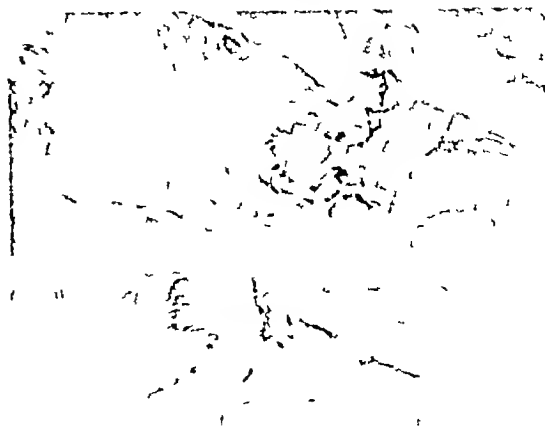


Fig 13 Case III The muscularis mucosae is split and its fibers enter the tumor. The submucosa follows the muscularis mucosae partly to form the stroma of the tumor.

microscopic picture showed the tumors to conform to the congenital type.

Case IV Chronic hypertrophic gastritis erroneously diagnosed polyposis or polypoid malignancy. J. I., a sheep raiser aged 36 years, complained of attacks of nausea and blood streaked vomiting. He was constipated for years. On July 18, 1938 following a light lunch he started to vomit and had been vomiting daily since that time. He often retched and developed a severe cramping pain in the lower abdomen. At the end of a period of retching there would be a few streaks of blood in the vomitus but at no time did he have a massive hemorrhage. In the past few weeks he had been vomiting almost constantly. On physical examination there was a def

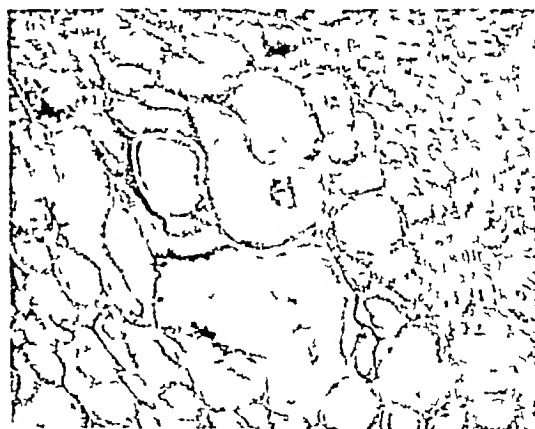


Fig 14 Case III Many of the gastric glands are dilated. Often the epithelial cells contain an abundance of clear cytoplasm suggesting the presence of mucus. The epithelium shows no striking change from the normal.



Fig. 5. Case IV. Nodular mottling of the lower two-thirds of the stomach outline producing the appearance of an irregular polypoid carcinoma. The roentgenological diagnosis as polypoid tumor of the stomach. The roentgenologist felt that the lesion was extensive, probably inoperable, true polypoid or an unusual sarcoma. Twelve weeks after x-ray therapy re-examination showed irregular defects extending to the cardia.

into area of tenderness in the midpigastrium. There were no masses and a rigidity. His hemoglobin was 80 per cent erythrocytes, 4,000,000 blood Wassermann and rhine were negative. He lost 5 pounds in the past 3 weeks. Patient refused gastric analysis but the vomitus showed an absence of free hydrochloric acid, and a total of only 7 there was a positive test for occult blood. The stool showed a positive test for occult blood on two occasions. Roentgenological examination showed a nodular mottling of the lower two-thirds of the stomach outline producing the appearance of an irregular polypoid carcinoma (Fig. 5). The roentgenological diagnosis was polypoid tumor of the stomach. The roentgenologist as of the opinion that the lesion was extensive, probably inoperable, a true polypoid or an unusual sarcoma.

The patient was given a course of x-ray therapy. Re-examination twelve weeks later showed multiple irregular nodular defects extending from the pylorus well up to the cardia. The appearance was that of a rather diffuse papillomatous new-growth. In view of the failure of the lesion to respond to radiation, surgery was advised.

Operation was performed on September 7, 1938. The abdomen was opened by one of us (H. B.)

Nothing abnormal could be felt in the stomach or duodenum except a slight thickening of the peritoneal wall. There was no induration, no enlarged glands. The spleen, liver, pancreas, and gall bladder were normal. Anterior gastrotomy revealed that the mucous membrane was thrown into high thickened folds with deep sulci between them. Most of these ridges ran longitudinally but one fold about one half inch wide ran obliquely posteriorly. There was no sign of polypoid tumor anywhere in the stomach. The ridges were from 1 to 1½ centimeter in height and had a normal pink color before manipulation. Here and there in the sulci there were small, round, soft or circumscribed reddish areas about 4 millimeters in diameter which were probably areas of gastritis. Except for this the sulci were pale pink. A large amount of mucus covered the entire mucosal surface of the stomach. The ridges were highest in the pylorus and midportion to the stomach, gradually becoming thinner and lower as the cardia was reached. There was no bleeding from the mucosa.

It was impossible to make a definite diagnosis at the time of operation but, in view of the history and other findings, subtotal gastrectomy was done. Inspection of the cardiac stump showed that the mucous membrane was found to be moderately hypertrophic with some prolapsing of the mucosa of the anterior wall. There were no polypoid tumors. About 1 inch of the anterior wall of the gastric stump, which contained the hypertrophic mucous membrane, was removed in addition to the part of the stomach previously resected. The patient made an uninterrupted recovery.

*Examination of surgical specimen.* Figure 17 is a drawing of the specimen and gives good idea of the



Fig. 6. Case IV. Chronic hypertrophic gastritis. The glands are tortuous, some are branching. Many are dilated, forming cysts, some of which contain plasma cells and red blood cells. In the interstices between the crypts are plasma cells, eosinophils, and lymphocytes. The epithelial cells are often high and cylindrical, containing considerable mucus, those lining some of the cysts are flattened. The mucosal surface is covered with a layer resembling fibrin.



Fig 17 Case IV Hypertrophic gastritis erroneously diagnosed as polyposis or polypoid malignancy

gross pathology. In short, the resected portion of the stomach showed a marked hypertrophy of the mucous membrane which was thrown into large folds. The description of the stomach at operation was exactly the same as that found in the resected portion.

The photomicrograph, Figure 16, reveals evidence of a chronic hypertrophic gastritis of severe grade without any evidence of papilloma formation. The detailed report of microscopic examination follows.

In many portions of all sections the surface epithelium is missing. The pits are extraordinarily elongated, partly corkscrew-like, branching and showing cystic enlargement in quite a few areas. The epithelium of the crypts is cylindrical and high. However, some of the cysts have a very flat, compressed epithelium. In the interior of the cysts many plasma cells and red blood cells are seen. The interstices between the elongated pits contain plasma cells and eosinophils. The body glands are normal, but at some places the cysts are so large as almost to reach the muscularis mucosae and to replace the body glands entirely. There is slight infiltration in the submucosa but not in the muscularis. Some lymph follicles penetrate through the muscularis into the submucosa. Extensive hemorrhage seen in the submucosa may be artificial. However, in slide 3 the

superficial capillaries are enlarged and in one place the cystically enlarged pits are covered with blood at the surface, which does not seem to be an artefact as signs of organization (strands of fibrin) are visible.

Microscopic diagnosis: severe proliferative, cystic hemorrhagic chronic gastritis.

The history and x-rays findings in this case were considered diagnostic of an intrinsic lesion of the stomach probably either a polyposis or a polypoid malignancy. To the surprise of everyone a marked hypertrophic gastritis was found in the resected stomach. This case is very similar to a case previously reported by Brunn and Pearl in which the same error was made. In both cases polypoid lesions were diagnosed but the pathological lesion proved to be chronic hypertrophic gastritis.

#### SUMMARY

This report is an analysis of 41 cases of gastric polyposis having 3 or more polyps, in-

TABLE III.—CASE DATA

TABLE III.—CASE DATA																							
Case, date reported, age and sex	Author	Method of making correct diagnosis	Invasive method	Hereditary polyposis	Duration	Symptoms							Physical signs			Roentgen analysis					X ray	Treatment	
						Pain	Anorexia	Nausea	Vomiting	Diarrhea	Intestinal obstruction	Weight loss	Constipation	Tumor	Intestinal	Rigid	Loss HCl	Total HCl	Intestine	Colon			X-ray changes
1927 G	Carver and Wright	P.M.			1000	+	+	0	+	+	+	+	+	+	+	0						Diagnosis by roentgen No invasive exam	Medical
1928 M	Mason and Dwyer	Operation			21 yrs					+												One year ago started New onset disease	Continuing Examine post
1928 F	Stewart, Meyer and Bloom	Operation			370	-	+			+			0	+	0	0	12	+		+	+	No previous Characteristic polyps of colon	Adenoma polyp biopsy
1928 M	Stewart, Meyer and Bloom	Operation			370	+							0	0	0	0		0				Normal polyps defective diagnosis biopsy	Colitis caecalis
1928 M	Latham	Operation			1000	+								+								Clear no lesion initial roentgen	Continuing Biopsy
1929 G	Latham and Fennell	Operation			1000	+	+				+		0	0	0			0				Single defect polyps	Continuing Biopsy
1930 G	Ackman	X ray			370					+	+		+		0	18		0		+		Following defect upper third greater col vagina and polyps Intestine diagnosis cap inspiration of intestinal peristalsis	Partial gastrectomy and duodenal biopsy
1930 G	Walker, Flannery and Wright	Operation			1000	+		0	0				0		0							No defect antrum	Continuing Examine post
1930 F	Walker, Flannery and Wright	Surgical specimen			370	+	0	0	+				+	0				+				Lesion of greater curvature, border removal, biopsy postulated	Gastric resection
1931 G	Kennel	X ray			1000	-	-	+							0	24						3-4 filling defects in upper antrum	Continuing Biopsy post
1931 G	Kennel	X ray			370	+	-	+	+						0							Filling defects Lower postulated	Biopsy postulated

\*Mason's trouble 370.

†10 spec.

TABLE III—CASE DATA

Course	Part involved						Number of tumors	Pathological diagnosis	Clinical diagnosis	Urine	Anemia	Occult blood-stool	Blood Wassermann	Weight loss (lb.)	Chronic inflammation	Malignant degeneration	Coincident involvement	Remarks
	Upper 1/3	Middle 1/3	Lower 1/3	Greater curvature	Lesser curvature	Anterior wall	Posterior wall											
Death in 2 days from hematemesis				+		+		18	<i>Polyadenome polypeaux</i>	None	-				0	0	0	Vague indigestion 35 years ago — for 3 years abdomen very distended jaundiced for 6 wks. At p m 4 000 c c bile-stained ascites. Large amount old and recent blood in stomach. Gastric mucosa atrophic but wall hypertrophied. Carcinoma of pancreas with pulmonary metastases
No diarrhea since operation	+	+					+	5	Benign polyps	Polyps		0		+		0	0	Presenting symptom — diarrhea of 25 yrs standing 3 tumors on x ray 5 at operation
No relief from Sippy regimen before operation. Uneventful convalescence after operation	+	+	+	+		+	+	Numerous	<i>Polyadenome en nappe</i>	Intrinsic gastric lesion probably malignant		0		-	+	0	0	Markedly hypertrophic mucosal rugae at times 5 cm deep Onset with sudden pain and hematemesis
Blood picture 10 months after operation resembled pernicious anemia	+	+	+					Numerous	<i>Polyadenome en nappe</i> Hypertrophy gastric glands	None		*	0		+	0		No clinical diagnosis in report
Well 3 yrs after operation	+	+	+	+	+	+	+	Many	Adenomatous polyp with probable malignant degeneration	Ulcer					+	+		Entire gastric mucosa covered with vegetations Resection impossible. At operation stomach normal on first examination
5 mos. after operation dizziness and heart trouble transient jaundice	+		+	+	+	+		3	Adenocarcinoma	Gastric tumor	-	0		-		+		Resection impossible. Tumors missed by barium meal were found by pneumogastrogaphy X ray showed pyloric polyp overlooked 2 polyps in upper stomach
No symptoms x yr after operation	+	+	+	+	+	+		9	Multiple adenopapillomas ( <i>en nappe</i> ) carcinoma	Papillomas of stomach and duodenum with malignancy		+		10	+	+		Initial symptom severe gastric hemorrhage. Polypoid mass prolapsed into duodenum without obstruction Liver enlarged. Blood pressure 260/110 Toxic adenoma of thyroid
3 mos. after operation recurrence of pain x rays negative, still no free HCl			+				+	3	Polyps carcinoma	Polyp or carcinoma		0		-	30		+	Diagnosed carcinoma of stomach in 1917 Stomach and duodenum normal at operation in 1920—appendectomy performed Achlorhydria 1920-1926 No anemia
3 mos. after operation slight gastric residue 6 mos. after weight gain 20 lbs. 1 yr after mass in left lower quadrant enlarged liver (?) malignancy		+	+	+	+			3	Adenoma and adenocarcinoma	Probable carcinoma		+		-	25		+	Diarrhea presenting symptom Increased mucus in stool
Death 2 days after operation from peritonitis		+						10	Adenomatous polyps	Polyp or carcinoma		+				0	+	4 defects by x ray 10 tumors at operation
		+	+		+	+		4	Polyps No malignancy	Polyps No malignancy			**	26	+	0		2 defects by x ray 4 tumors at operation

\*Severe like pernicious anemia

†Probable

‡Moderate

§In large polyp

¶Small rectal polyp

\*\*Melena

TABLE III—CASE DATA—Continued

Case, date reported, age and sex	Author	Method of making correct diagnosis	Encephalic abnormality	Dura	Symptoms										Physical signs					Gastroc analysis					X-ray	Tissue
					Pain	Seizures	Abnormalities	Weakness	Paralysis	Deafness	Blindness	Stupor	Coma	Convulsions	Tumor	Tenderness	Right	Left	Total	Protein	Glucose	Urea	Chloride	Myelin		
1431 J	Kennet	X-ray		1/2 inch	+	+	+	+	+	+	+	+	+	+											General picture of brain	Gastroc normal
1432 H	Kennet	X-ray		37	+																				Many defects	Extensive gliosis
1433 M	Kennet	X-ray		mm.	+	+								+											Many defects seen	Extensive gliosis
1434 H	Beckham	Osteotomy		37	+		+																	+	Many irregular defects	Extensive gliosis
1435 F	Hobbs	X-ray	+	mm.	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Many defects	Extensive gliosis
1436 J	Kennet	Osteotomy		37										+											Multiple gliosis	Extensive gliosis
1437 M	Palmer	P.M.	+	mm.	+	+	+	+	+	+	+	+	+	+												
1438 M	Kuchner	P.M.	+	7	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		Extensive gliosis
1439 F	Beckham	Surgical specimen	+	14 yrs	+	+	+	+	+	+	+	+	+	+										+	Extensive gliosis	Extensive gliosis
1440 H	Beckham and Allen	Osteotomy		mm.	+	+	+	+	+	+	+	+	+	+											Large defect in posterior wall of upper third and mid 3rd	Extensive gliosis
1441 M	Beckham and Allen	P.M.		37	+	+	+	+	+	+	+	+	+	+											Large defect in posterior wall of upper third and mid 3rd	Extensive gliosis
1442 M	Beckham and Allen	X-ray		6 mm.	+									+											Multiple defects in granular cortex	Extensive gliosis
1443 M	O'Brien	X-ray		37	+	+	+	+	+	+	+	+	+	+											Many gliosis	Extensive gliosis

\*In spec    † weeks after operation    ‡ 12a vomitus    § 6 years after operation    ¶ etc

TABLE III—CASE DATA—Continued

Course	Part involved						Number of tumors	Pathological diagnosis	Clinical diagnosis	Urine	Anemia	Occult blood stool	Blood Wassermann	Weight loss (lb.)	Chronic inflammation	Malignant degeneration	Coincident involvement	Remarks
	Upper 1/3	Middle 1/3	Lower 1/3	Greater curvature	Lesser curvature	Anterior wall	Posterior wall											
Death 3 days after operation from anemia	+	+						Many	Polyposis. Medullary carcinoma	Possible malignancy	*	+				+		No gastric symptoms
Death 1 day after operation from pulmonary edema		+	+				+	5	Polyposis Papillary carcinoma. Pernicious anemia	Benign polyps		†		33		+		Blood picture like pernicious anemia Slight icterus 4 mos duration paresthesia of extremities 2 filling defects on x ray 5 tumors in stomach at operation
Death 4 wks. after operation from hemorrhage despite repeated transfusions	+	+	+	+	+	+	+	Many	Papillomas adenocarcinoma	Polyposis	+	+	†		+			Severe anemia Malignancy not demonstrated in surgical specimen but definite at autopsy
	+	+	+	+	+	+	+	Many	Polyadenoma en nappe Chronic gastritis	Diffuse infiltration gastric wall probably benign					+	○		Resection not possible. Definite invasion of submucosa, but no atypical abnormal staining or mitosis
Death 4 days later of cerebral embolism (?) ileus or acute dilatation of stomach		+	+					Many	Polyposis with malignancy	Carcinoma of stomach or esophagus	++ §	+	+	40		+		Duodenal involvement questionable
Gained 16 lbs. 6 wks. after operation							+	5	Benign polyps	Carcinoma	+	†		+		○		Too weak to stand gastric resection
Death No operation	+	+	+	+	+	+		7	Polyps (inflammatory hyperplasias)	None antemortem					+	○		Atrophic—hypertrophic gastritis of entire mucosa
Delirium and death 5 days (?) alcoholism	+			+				3	Polyposis with malignancy	None		+			+	+		Malignancy in one polyp only Alcoholic hallucinosis cachexia
Completely relieved of symptoms	+	+	+	+	+	+	+	Many 40 polyps per sq in	Polyposis	Hour glass stomach	○		—	+	+	○	○	Almost complete obstruction of pylorus by polyp
Relieved for 5 yrs Then re-operation for polypoid masses. Death from peritonitis	+	+	+	+			+	First operation—5 2nd many	Polyposis Adenocarcinoma	Probable malignancy		+	+	15		+		Condition did not warrant resection of stomach at 2d operation
Death after 33 days	+	+	+	+	+	+	+	group	Polyps Adenocarcinoma	Carcinoma				20		+	○	Blood culture positive for Streptococcus viridans 2 carcinomas probably developing from benign tumors
No symptoms 7 mos. after operation	+	+	+	+	+	+	+	Over 100	Adenomatous polyps	Polyposis		+	+	30	+	○		Frozen section of 3 polyps at operation
Relief	+	+	+	+	+	+	+	Many	Polyposis with malignancy	Fibrosarcoma or benign polyposis	○			○		+	○	Carcinoma in one area. Metastatic gland in lesser omentum

\*Severe †Melena ‡Marked §Alb



TABLE III.—CASE DATA—Continued

Case, date reported, age and sex	Author	Method of making perfect diagnosis	Examine alcohol	Hereditary polyposis	Duration	Symptoms							Physical signs			Gastric Analysis				X ray	The end			
						Pain	Anorexia	Nausea	Vomiting	Diarrhea	Hemorrhage	Weight loss	Constipation	Tumor	Tenderness	Regularity	Free HCl	Total HCl	Free acids			Mixed	Tumor found	Myomata
5 1915 M	McRoberts	X-ray			8 yrs	+			0					0	0	0							polyps on posterior wall	Polyps removed
10 1915 M	McRoberts	Surgical specimens			200	+	0	0	0	0	+	+											Dendritic ulcer	Partial resection and further study
17 1915 M	McRoberts	Surgical specimens			17 yrs	+						+		+			8	13					No ulcers	19.10.15 per 2 per specimen
18 1915 M	McRoberts	Operation			10 yrs	-	+	+	+	0	+		+			19.4	8		+				hypercarcinoma, lower 1/3 of body of stomach	19.4 removed and sent for study
																							hypercarcinoma	
																							19.4	12
19 1915 M	Ravenscroft	X-ray			7 yrs	+		0	0			+	+	+	0				+			Multiple 2" long defects	Complete gastric resection	
20 1915 F	Pandey and Andrew	X-ray			(?)	0	0	0	0	0						8 to 10	10 to 10					Marked by resection (cancer) filling defect of no tumor, cancer (cancer) ulcer small defects	Gastric resection, polyps, pyrometastasis	
19.96 1916 M	Van Bantick	X-ray			27	+			+	+						0							Multiple polyps	Gastric resection
21 1916 M	Van Bantick	X-ray			(?)	+			+	+			+			8	8						Multiple defects in upper stomach and first part of duodenum	
22 1916 M	Forrest	X-ray			7 yrs	-	0	0	0	0			0	0	0	0							Multiple 15 mm defects, carcinoma and dendritic ulcer	Gastric resection (1916)
24 1916 M	Paperna	X-ray			(?)	+	0		0	+			0	0		0							Multiple 15 mm defects, carcinoma, anaplastic thickened	19.10.16 resection of stomach
25 1917 F	Holman	Operation			10	+								+	+	+								Resection of stomach and first part of duodenum
26 1917 F	Holman	X-ray			7 yrs	+																	Multiple gastric polyps	Resection of stomach, 19.10.17 resection of stomach

\*Clear symptoms. †Tumor. ‡No gastric complaints. §Not done.

TABLE III—CASE DATA—Continued

Course	Part involved						Num ber of tum ors	Pathological diagnosis	Clinical diagnosis	Urine	Anemia	Occult blood stool	Blood Wassermann	Weight loss (lb.)	Chronic inflammation	Malignant degeneration	Coincident involvement	Remarks
	Upper 1/3	Middle 1/3	Lower 1/3	Greater curvature	Lesser curvature	Anterior wall	Posterior wall											
		+	+				+	Many	Adenomatous polyps	Polyps		○				○		
		+						Multi ple	Gastric ulcer Polyposis	Duodenal ulcer		+	+		+			Gastric resection for ulcer Polyps found in surgical specimen in addition to ulcer
			+					Multi ple	Multiple sessile polyps Chronic gastritis	Ulcer		+			+			Gastroenterostomy for multi ple ulcers 15 yrs ago cau tery excision high gastric ulcer and cholecystectomy 14 yrs ago relief for 5 yrs then ulcer symptoms
1926-1931—no symptoms Then recurrence of pain weakness and melena 1933— large carcinoma		+	+				+	3	Polyps. Carcinoma <i>in situ</i>	Carcinoma		+	+	17		+		No metastases in excised gland in 1926 In 1933 inoperable carcinoma with metastases to extragastric gland
Death 12 hrs after operation (pneumonia)	+	+	+	+	+	+	+	Large num ber	Benign polyposis	Diffuse polyposis		§	○	20	○	○		Spleen removed on account of bleeding. At p.m. stomach distended with blood
Death 1 year after operation			+					Sev eral	Polyps	Multiple pro lapsing polyps			—	18				Stomach negative to palpa tion at operation. Polyps attached to redundant gas tric mucosa found on gas trotomy
	+	+	+	+	+	+	+	Many	No specimen	Multiple polyposis								Vomited 2 tumors on one oc casion Stomach wall cov ered with many small polyps
Well for 1 yr Then return of symp toms and large palpable mass. Died 2 yrs. after operation of carcinomatosis	+	+	+	+	+	+	+	Many	No specimen	Multiple polyposis						+		Entire stomach and first part duodenum covered with pol yps (Note duodenal in volvement.) (See text)
Well 4 yrs. after operation X-rays repeatedly negative			+				+	Multi ple	Adenocarci noma. Multiple polyps	Prolapsed gas tric polyps with probable malignancy	—	§	—			+		Polyps prolapsed into duode num
Complicating subphrenic abscess Death in 2 wks				+				Sev eral	Polyposis ventriculi circum scripta	Polypoid carcinoma	§	○	—			○		Multiple degenerative proc esses in central nervous sys tem
Well 15 mos after operation	+	+	+	+	+	+	+	Multi ple	Polyposis Hypertrophic gastritis Duodenitis	Surgical abdomen						○		Operation for acute perfora tion of duodenal ulcer Stom ach filled with polyps Spec imen shows polypoid folds up to 1 inch thick, abruptly ending at duodenum In flammation of duodenum
	+	+					+	Sev eral	Polyposis with malig nancy	Multiple gastric polyps	—	+	**	+	††	+		Diagnosed pernicious anemia

\*Large tarry stools †Mild ‡Melena tarry stools §Slight ¶Albumin trace \*\*Constant ††Marked

TABLE III.—CASE DATA—Continued

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Case, date or period, age and sex	Author	Method of making correct diagnosis	Previous alcohol	Hereditary polyposis	Duration	Symptoms										Physical signs			Gastric analysis					X ray	Tumors	
						Pain	Anorexia	Nausea	Vomiting	Diarrhea	Constipation	Weight loss	Emaciation	Tenderness	Regurgitation	Free HCl	Total HCl	Free trypsin	Alcohol	Tumor tissue	Myocardium					
37-37 M	Christopher	Operation			yr.	+	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0	0	0	0	"Large carcinoma of body"	Continued to total P. on 100 lbs.
38-38 F	Chen	Operation	0		yr.	+	+	+	+	0	0	+	+	0	0	0	0								No report	Increased weight, 100 lbs.
39-1944 M	Pearl and Brown	P.M.	0	0	yr.	+		+	+	0	0		+	0	0	0	0								No. size of stomach, diffuse polypoid cancer	Remains in a strong and active state
40-1945 F	Pearl and Brown	P.M.	0	0	yr.	+			+																100 — Dumping gastric contents. Normal stomach	No weight gain, gastric symptoms
41-1945 M	Pearl and Brown	Surgical specimens	0	0	12	0	0	+	+	0	+	+	+	+	0	0	0	0	0	0	0	0	0	0	100 — Intestine, stomach contained food and feces, contracting bands at pylorus. Diagnosis: carcinoma of stomach	Subtotal gastrectomy

Lip gastric polyps decreased. 11 Digestive symptoms such type at age years

cluding 3 new personal cases. It is supplementary to a previous report of 84 cases published by Brunn and Pearl in 1926.

Multiple gastric polyposis may be congenital (neoplastic) or inflammatory (hyperplastic). The two types may often be differentiated on gross examination alone. On microscopic examination one finds that in neoplastic polyps the muscularis mucosae enters the tumor for a variable distance and usually be-

comes fragmented or split, with the submucosa entering the tumor for a variable extent. In the hyperplastic types the muscularis mucosae is intact and forms a delineating membrane the submucosa playing no part in the formation of the tumor. Borderline cases may be difficult to classify.

The symptoms are not characteristic. In the series, epigastric pain and tenderness were most frequent. In over half of the cases,

TABLE III—CASE DATA—Continued

Course	Part involved						Number of tumors	Pathological diagnosis	Clinical diagnosis	Urine	Anemia	Occult blood stool	Blood Wassermann	Weight loss (lb.)	Chronic inflammation	Malignant degeneration	Coincident involvement	Remarks
	Upper 1/3	Middle 1/3	Lower 1/3	Greater curvature	Lesser curvature	Anterior wall	Posterior wall											
10 lbs increase in weight 4 mos later	+	+	+	+	+	+	+		Diffuse adenocarcinomatous metaplasia. Polypadenoma en nappe	Carcinoma of stomach	-		-	12	+	+	Q	Unusually diffuse carcinomatous involvement
Death from liver after 9 operations for polyps and their complications	+	+	+	+	+	+	+	Many	Gastrointestinal polyposis	Gastrointestinal polyposis	*			†		○	+	In 1918 at age 20 excision 4 duodenal polyps and gastroenterostomy for pain and severe bleeding diagnosed as duodenal ulcer and amebic dysentery. In 1919 resection 3 feet of ileum for intussusception, 3 polyps in specimen. In 1928 second intussusception not requiring resection opened ileum showed 5 polyps which were excised. In 1929, fulguration rectosigmoid polyps 1 mo later large polyp removed from cecum was diagnosed adenocarcinoma. In 1930 anastomosis transverse colon to sigmoid and left colectomy. In 1937 operation for pyloric obstruction showed multiple polyposis entire stomach too ill for gastric resection. Endotherm snare excision numerous polyps through Janeway gastrotomy. Liver death.
Death 10 days after operation from peritonitis	+							Many	Polyposis of stomach and colon	Polyposis of colon		+		4		○	+	Fresh blood recovered from stomach tube treating intestinal obstruction
Death from cardiac failure	+	+	+	+	+	+	+	50-100	Polyposis of stomach and large bowel	Diaphragmatic hernia of stomach		○	-			○	+	Syphilitic history but blood Wassermann and cerebrospinal fluid negative. Polyposis diagnosed in retrospect examination of films
Death 5 days after operation with jaundice peritonitis and terminal pneumonia	+	+	+	+	+	+	+	Large number—over 100	Diffuse polyposis with adenocarcinoma of antrum	Carcinoma	±	SI	+	-	15	+	+	Gastroscopy showed polypoid excrescence in antrum and in body diffuse nodular process of body, impression—diffusely infiltrating carcinoma. The essentially diffuse nature of the multiple polyposis was not noted on gastroscopy

\*Hb 38% in 1918 †Marked ‡Albumin trace §40 RBC N D F ¶Colon bladder

bleeding was found to take place in the vomitus, stool, or gastric content. Pedunculated tumors and those near the pylorus are more apt to give symptoms of separation of polyps or pyloric obstruction. Some patients have had symptoms over 20 years. The physical findings are indefinite and may be entirely lacking.

The diagnosis is attended with considerable difficulty. The x-ray may fail to differentiate

multiple polyposis from chronic hypertrophic gastritis, retained food, bezoar, or sarcoma. The correct diagnosis was made most often by x-ray and by operation, but the condition was often overlooked by the roentgenologist. Gastroscopy is a valuable aid in the diagnosis of gastropathies, especially in the differentiation between benign and malignant lesions, and between polyposis and hypertrophic gastritis. Both methods are complementary and their

combined use will greatly enhance our diagnostic acumen

Free hydrochloric acid was absent from the fasting gastric content in almost every case. Careful search should be made in the gastric content for tumor particles which may establish the diagnosis.

In our previous series malignant alteration was noted in 12 per cent. Of the present series of 41 collected and personal cases since 1926 4 gave no malignancy data. Of the remaining 37 malignant alteration was found in 19. This alone argues for radical surgical removal of the tumor bearing area by gastric resection as soon as the diagnosis is made and the patient is properly prepared. Further confirmation for this policy is afforded by the separate analyses of a small number of benign and malignant cases in which patients were treated either by excision of polyps or by gastrectomy; these show a great superiority of results in gastrectomized subjects.

#### REFERENCES

1. ACHESON, F. D. *Cancer* 31 Am J. 320, 3 30
2. ARNDAL, G. *Treatise on Pathological Anatomy* 812. English translation from the French.
3. AUCHINCLOSS, W. and KOPPELBERG. *Dent. Chir.* 9 6 364
4. BAIRD, S. *Surg. Gyn. Obst.* 9 4, 22 105.
5. BAKER, G. *Kilburn med.* 912 48 985
6. BAKER, E. B. and ALLEN, A. W. *Surg. Gyn. Obst.* 934, 18 79
7. BLAND-SUTTON, J. *Lancet, Lond.* 1903, 1.
8. BOERHAAVE. *Das Wachstum und die Vertheilung des Magencarcinoms* Jena, 90 (Quoted by HALL)
9. BRAND, W. A. *Med. Chir. N. America*, 924, 7 332  
BRET J. *Arch. gen. med.* 903, 345-350  
Case abstract from the original by Physicians Research Bureau, New York City
10. BRIMM, E. *Arch. gen. med.* 885, 16 57
11. BROWN, M. R. N. *England J. M.* 934, 0 473
12. BRYAN, H., and FRANK, T. *Surg. Gyn. Obst.* 910, 43 350-368
13. Idem. *Am. J. Surg.* 957 40 5
14. BAUMANN, A. SCHMIDT, R. L. and RABENHORN R. *J. Nat. Cancer Inst.* 94 45
15. BRYAN, L. *Southwest Med.* 9 2 6 3-227
16. CANNON, R. G. and WRIGHT SMITH, R. *J. Med J. Australia*, 9 7 58
17. CAMPBELL, A. M. *Surg. Gyn. Obst.* 9 30 66
18. CANNON, R. D. *Recent Progress of Diseases of the Alimentary Canal* 2d ed., 57-272. Philadelphia W. B. Saunders & Co. 930.
19. CANNON, R. D. *Ueber zwei Facien von seltenen Magencarcinomen. Beitr. path. Anat.* 9 2, 54 503  
CANNON, R. D. *Arch. Surg.* 937 06 39
20. COLLIER, WILLIAM T. *Path. Soc. Lond.* 806, 47 45
21. CONNELL. *Bull. Soc. anat. Paris*, 86, 51 51
22. Idem. *Gaz. Med.* 94, 77
23. CURY, J. M. *Arch. Anat. Pathol.* 912, 1 100
24. Idem. *Tratado de anatomia patologica* 1912, 1 100
25. DUBOIS, C. *Arch. Clin. Chir.* 1912, 1 100
26. DUBOIS, H. *Arch. Clin. Chir.* 907 13 100
27. DUBOIS, J. *Ann. Surg.* 912, 77 100-104
28. DUBOIS, E. R. *Arch. Int. M.* 930, 10 100-104
29. EMMERT, W. *Arch. Anat. Physiol.* 1884, 9 51
30. FISCHER, E. L., and WRIGHT, V. M. W. *Surg. Gyn. Obst.* 925, 4 46
31. EMMERT, C. P. and SEXTY, E. G. *Surg. Gyn. Obst.* 922, 31 3
32. FROST, S. *Cancer and Other Tumors of the Stomach*, p. 30. London, 1902.
33. FISCHER, J. *Zentralblatt* 912, 1
34. Idem. *Bull. Clin. Woch.* 912, 1 100
35. Idem. *J. Am. M. Ass.* 912, 60, 1077
36. Idem. *Fortschritte Unternehmungen der Wissenschaften* 912, 51 040-050
37. FRYAN and FRIEDENWALD. *Am. J. M. Sc.* 1907 54, 683
38. GUTHRIE. *De cancer precoci de l'estomac* Dares laillon, Berna, 904. (Quoted by HALL)
39. GUTHRIE, F. *Arch. Verdauungsorg.* 1912 13 100
40. GLASS, F. A. *Oklahoma State M. J.* 904, 53
41. GODDARD, W. *Arch. Pathol.* 907, 10 100-104
42. HALL, J. E. *Am. J. Surg.* 912, 13 66
43. HALL, W. E. *J. Am. M. Ass.* 1912, 10 100-104
44. HALLER, G. *Ueber Polypen (Acidoselektische Tumoren und deren Beziehung zur Krebsentstehung)* *Deut. Arch. Klin. Med.* 905, 11 49
45. HALLER, H. *Ueber Polypen (Acidoselektische Tumoren)* *Deut. Arch. Klin. Med.* 905, 11 49
46. HALLER, G. *Arch. Surg.* 912, 13 66-954
47. HALLER, G. C. *Lancet*, 1912, 13
48. HALLER, G. W. *Am. J. Surg.* 1912, 13 66-954
49. HALLER, G. W. *Surgery* 912, 77
50. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
51. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
52. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
53. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
54. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
55. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
56. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
57. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
58. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
59. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
60. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
61. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
62. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
63. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
64. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
65. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
66. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
67. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
68. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
69. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
70. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
71. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
72. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954
73. HALLER, G. W. *Arch. Anat. Physiol.* 1912, 13 66-954

74. MILLER, T G, ELIASON, E L, and WRIGHT, V W M Arch Int. M, 1930, 46 841
75. MILLS, G P Brit. J Surg, 1922, 10 226-231
76. MONFALCON Dict. d sc med Par, 1820, 44 227
77. MOORE, A B Am. J Roentg, 1924, 11 61-66
78. MYER, J S J Am M Ass, 1913, 61 1960
79. NAPP, O Ueber die Bildung polypoiser Adenome und Carcinome in atrophischer Magenschleimhaut. Freiburg, 1900
80. NEUMANN, B Arch klin Chir 1932, 171 790
81. OSCHSNER, H C, and MASON, R N J Indiana M Ass, 1933, 26 427
82. OCHLECKER, F Beitr klin Chir, 1934, 160 1
83. ORTH. Lehrbuch der speciellen pathologischen Anatomie 1887, 1 709
84. OTTO, WILHELM Auswuechse im Magen durch ein Stueck Holz verursacht Neue seltene Beobachtungen zur Anat u Physiol, 1824 Quoted by Watanabe
85. PENDERGRASS, E P, and ANDREWS, J R. Am J Roentg, 1935 34 337
86. PERKLE, L L J M Soc N Jersey, 1936, 33 615
87. PETIT, G, GERMAIN, R, and BRENTON, F Bull Soc anat. Paris, 1907, 82 554.
88. PETROW Zbl Chir, 1896, p 543
89. PORT, K Deut. Zschr Chir, 1896, 42 181
90. PLONSKIER, M Zbl allg Path 1932, 54 49
91. POPOVIC, S Fortsch Röntgenstrahl, 1936, 53 341
92. RHOADES, C P J Nat Cancer Inst, 1941, 1 511
93. RICHARD Soc Anat, 1846, July
94. RIPAULT Bull Soc anat. Paris, 1822, p 61
95. RIPPERT Fragenzung zur Geschwuelstlehre Bonn, 1907 (Quoted by Heinz)
96. ROCHESTER. Buffalo M & S J, 1869, 8 167
97. ROSENBACH and DISQUE Arch klin Chir, 1923, 124 2848
98. RUGGLES, H. E Unusual gastric polyp Am J Roentg, 1920, 7 356
99. SCHINDLER, R. Münch med Wschr, 1922, No 15
100. Idem Arch Int. M, 1923, 32 635-646
101. Idem J Nat Cancer Inst, 1941, 1 451
102. SINCLAIR, N Brit J Surg, 1933, 20 645
103. SKLIPOSSOWSKI Virchows Arch, 1898, 153 130
104. STEVENS, J B Glasgow M J, 1896, 45 422-424.
105. STEWART, H L J Nat. Cancer Inst, 1941, 1 489
106. STEWART, M J J Path Bact., Lond, 1913, 18 127
107. STONER, W C Ohio S M J, 1914, 10 747
108. STRAUS, A, MEYER, J, and BLOOM, A. Am J M Sc, 1928, 176 681
109. STRUTHERS, J E Surg Gyn Obst., 1924, 38 610-624
110. TESSIER, R Med Klin 1933, 29 22
111. VAN BUSKIRK, E M J Indiana M Ass, 1936, 29 218
112. VERSE, M Arb path Inst. Leipzig, 1908, 1 175
113. WALTERS, W Proc Mayo Clin, 1933, 8 315
114. WASSINK, W F Ned tschr geneesk., 1916, 2 2199
115. Idem Ned tschr geneesk., 1916, 2 1108-1116
116. WATANABE, R Arch. Verdauungskr, 1901, 15
117. WECHSELMANN, L Beitr klin Chir, 1910, 70 855-909
118. WEGELE, C Mitt Grenzgeb Med Chir, 1909, 19 53
119. WINTERNITZ, M D, and BOGGS, T R Bull Johns Hopkins Hosp, 1910, 21 203

# DEVELOPMENT OF THE VERTEBRAL COLUMN AS RELATED TO CERTAIN CONGENITAL AND PATHOLOGICAL CHANGES

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**A** THOROUGH knowledge of the embryology of the vertebral column is essential for understanding diseases of the spine. In addition to obvious malformations many lesions of later life are based on the complex development of the involved structures. It is the purpose of the present paper to discuss the development of the vertebral column and to point out the embryologic basis of certain confusing lesions encountered in patients. Abnormalities of the neural arch do not fall in the scope of this study.

Most embryologists agree that the notochord is derived from the ectoderm forming the chordal plate and very early comes to lie between the medullary canal and the gut (Fig. 1). This notochordal plate is very rapidly surrounded by a condensation of mesenchymal tissue. It finally forms a long rounded structure extending from the hypophyseal pouch to the tail end of the spine. This chorda is the central structure around which the entire development of the spine occurs. The surrounding mesenchyme forms the perichordal sheath. The mesenchymal tissue also forms the segmented appearing sclerotomes. These consist of a zone of dense caudally situated and a less dense cranially situated zone of mesenchymal cells. The dense zones were called protovertebrae by the early embryologists; a better term is scleromere. Between the dense and the less dense portions a fissure occurs, the fissure von Ebner or intersegmental fissure (Fig. 2). Very early the dense zone (scleromere) forms three processes which extend dorsally ventrally and medially. The dorsal extensions form the mesenchymal anlagen of the neural arches; the ventral processes form the ribs or lateral processes and the medial or chordal extensions toward the notochord fuse with the

perichordal sheath. Later the chordal processes meet around the notochord and form the anlage of the primitive vertebral body. Very early the intersegmental arteries—branches of the primitive aorta—appear between the sclerotomes just caudally to the dense zone of mesenchymal cells. About this time definite membranous structures are formed by the less dense cranially situated portion of the sclerotomes. These membranes are the interlaminar and the intervertebral membranes connecting the neural processes and the ventral or costal processes. The caudal aspect of the dense very cellular portion of the sclerotomes then become hollowed out by the cranial portion of the next caudally placed sclerotome. At the same time some mesenchyme enters into this hollowed out area of the dense zone. This interposed mesenchyme together with the previously mentioned less dense mesenchymal zone of the sclerotome forms the anlage of the true vertebral body while the dense zone now displaced cranially forms the anlage of the annulus fibrosus and the intervertebral disc. The cranial shift is believed to be due to the presence of the intersegmental vessels and the increased nutritive which is available to the cells closest to these arteries. The primitive intervertebral discs now form a membrane which surrounds the anlagen of the vertebral bodies—this membrane is called the interlaminar membrane and it will form at a later stage the anterior lateral and posterior longitudinal ligaments of the spine. Coinciding with the formation of the interlaminar membrane the perichordal sheath forms a ventrodorsal extension which divides the true anlage of the vertebral body into two lateral halves.

Most embryologists agree that the true anlage for the vertebral body is formed by the interposed mesenchymes together with a portion of the dense zone of the sclerotome and

the less dense cranial half of the next caudal sclerotome. The fissure von Ebner then becomes the true dividing line between the final anlagen of the vertebrae. The intersegmental arteries are situated finally in the midportion of the vertebral bodies.

About the end of the fourth week the anlage of the vertebral body increases rapidly in size and the dense zone now representing the area of the future intervertebral disc becomes thin. The mesenchymal period ends there and the period of chondrification begins. The first centers of chondrification in the body proper occur laterally and are separated by the ventro-dorsal extension of the perichordal sheath. This membrane rapidly disappears as the chondrification process progresses.

The notochord, which has been unchanged during the development in the mesenchymal period and which has been present as a solid cord of even size throughout all the mesenchymal and early cartilaginous vertebral bodies and the zones of the annulus, becomes more and more squeezed into the regions of the



Fig 1. A human embryo, 3 weeks old, 6 millimeters in length. In the midsagittal section the notochord is well developed, *N*. At this stage the mesenchymal segmented tissue has not surrounded the notochord. The dorsal ectodermal layer, above, is well developed. The notochord has just differentiated from the ventrally situated entodermal tissue, below.

dense intervertebral discs (Fig 3). This is due to the increased pressure which prevails during the rapid enlargement of the cartilaginous

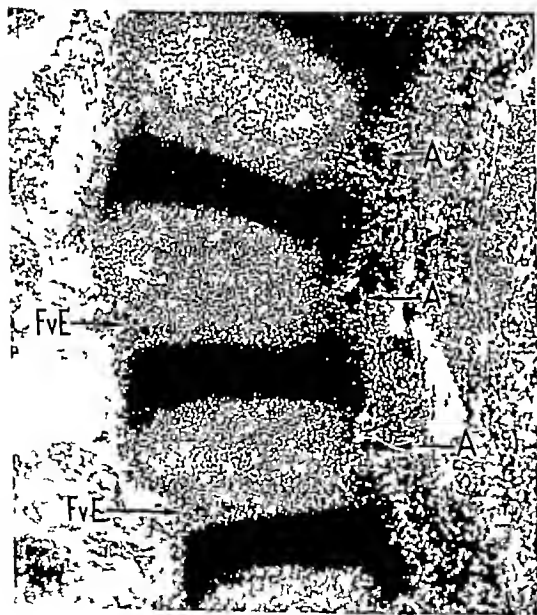


Fig 2. Four week (1.1 cm) embryo, showing dense and less dense portions of sclerotomes with hollowing out of the dense cranial portion by the less dense zone. Fissure von Ebner, *F v E*, well seen dividing the future vertebral bodies. Intersomitic arteries, *A*, seen situated in mid-portion of future vertebral body anteriorly.



Fig 3. Nine week (4 cm) embryo. Displacement of notochordal cells into disc zones, arrow, top. Persistence of mucoid streak. Vertebral vessels seen anteriorly, *A L*, Anterior longitudinal ligament, *A L*, attaching to vertebral bodies, posterior ligament, *P L*, to disc regions. Arrow, left, cartilaginous vertebral body. Note annulus fibrosus anlage.



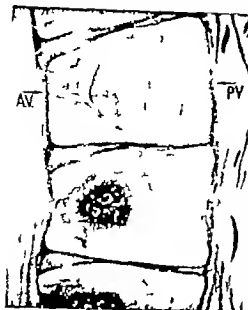


Fig. 4

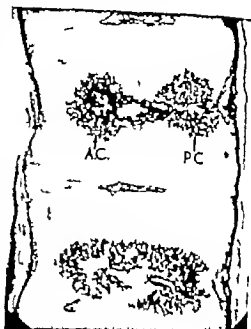


Fig. 5

Fig. 4. Four limb embryo (1 cm sitting height) on bryo, showing ingrowth of central  $A$  and dorsal  $P$  1 levels into cartilaginous vertebral bodies with early invagination of the cartilage.

Fig. 5. Four limb embryo (1 cm sitting height) on bryo. Position of the anterior  $A$  and posterior  $P$  1 association centers. Peritoneal levels are seen in the cartilage zones of the vertebral bodies.

Fig. 6. Seven and one half month (1.5 cm sitting height) fetus. Peritoneal levels are seen growing into cartilage plates. Osteons formation,  $O$  S T around the anterior and posterior roots channels. Cartilage remnant,  $C$  R, are vertebral body. Anterior longitudinal ligament,  $A$  L, not associated with intervertebral disc base but attached to vertebral bodies. Posterior ligament,  $P$  L, C R, F cartilaginous ring epiphysis attached to intervertebral disc tissue and not to vertebral bodies.

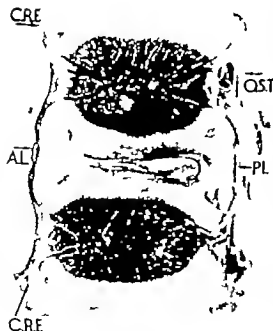


Fig. 6

vertebral bodies. The dense mesenchymal anlage of the annulus fibrosus becomes markedly reduced during the chondrification of the bodies and probably much of the primitive dense annulus actually undergoes chondrification. However the outermost rim of the disc always remains—dividing the cartilaginous vertebral bodies.

In a 7 to 9 weeks old (1.6-4 cm) embryo the cartilaginous cells in the center of the vertebral bodies are surrounded by interstitial matrix. At this stage the anterior and posterior longitudinal ligaments are developing and with a connective tissue stain some (17)

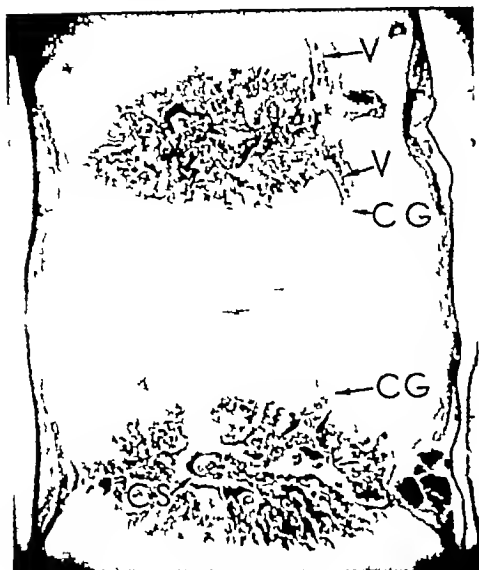


Fig 7

Fig 7 Five and one half month (19 cm sitting height) fetus Vessels, *V*, coming from vertebral spongiosa perforating cartilage plates Ring shaped cartilage remnant in one vertebral body, *C S*, *C G*, chondrification gaps

Fig 8 Seven and one half month (27 cm sitting height) fetus Well formed intervertebral disc and vertebral body Annulus fibrosus, *A F*, well developed Notochordal cells forming nucleus pulposus, *N P* Periosteal vessels *P V*, and vessels coming from vertebral body are visible. *x*, Line of endochondral bone formation with chondrification gap, *y*, line of endochondral bone formation

Fig 9 Schmorl's node, *S N* with rupture of cartilage plate, *C P* Protrusion of nuclear material into spongiosa Reactive bony cup and great amount of proliferating cartilage present

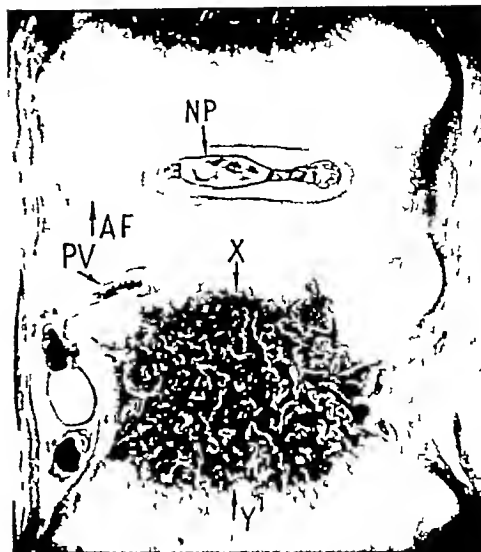


Fig 8



Fig 9

early collagen material is visible along the anterior band The cells in the region of the intervertebral disc arrange themselves in a fashion similar to the ones later seen in the annulus fibrosus Boehmig (2) states that the local vascular supply has some influence on the direction of growth of these cells The anterior longitudinal ligament at this stage is more attached to the cartilaginous vertebral bodies while the posterior longitudinal band is firmly attached to the intervertebral disc tissue and is not associated with the posterior surface of the vertebrae This point was emphasized by Schmorl (21), and it may have some importance in the development of osteophytes in late adult life

As chondrification of the vertebral body advances, nearly all the notochordal cells are

squeezed out from the body proper and are displaced into the disc region where they become enclosed by the dense rim of cells which have not undergone chondrification and which form the true annulus fibrosus The chordal cells during this period show some mucoid degeneration and some proliferation The notochordal tissue then forms the early nucleus pulposus

During this migration of the notochordal cells, the formerly rather thin annulus increases in height It is noteworthy that in this stage only the notochordal cells are displaced from the developing vertebral bodies



Fig. 10.

Fig. 10. Five and one-half month embryo. Bodian nerve fiber stain. Nerve bundles are seen within the anterior portion of the annulus fibrosus, arrow.



Fig.

Fig. 11. Five and one-half month fetus. Bodian nerve fiber stain. Arrow indicates a 1 inch nerve fiber.



Fig. 12.

are seen beneath the posterior longitudinal ligament. Fig. 12. Five and one-half month fetus. Bodian nerve fiber stain. Nerve fibers (arrows) are seen within the anterior portion of the annulus fibrosus and the cartilage plates accompanying the perosteal canals.

The perichordal sheath remains in the center of the cartilaginous vertebrae and forms the mucoid streak. Boettlich (3) has described some variations of the microscopic picture of the notochordal cells displaced into the annulus space as separation of cells into a cranial and caudal part divided by a membrane and also less often, a dorsal and ventral separation.

In the 9 weeks old embryo (4 cm.) anterior and posterior indentations into the cartilaginous body are produced by perosteal vessels and soon after this stage the cartilage is invaded by these vessels (Fig. 4). Calcification of the cartilage results and is well seen in the 3 1/2 month (9 cm.) embryo preceding the ossification process. The cartilaginous vertebral body is therefore the true foundation for the development of the osseous vertebral body. The invading vessels produce a ventral and dorsal blood lake. In the beginning the ossification centers which are formed dorsally and ventrally in the cerebral body are separated by a cartilaginous septum which persists for a short period of time (Fig. 5). At times this cartilaginous septum will take the shape of a ring (Fig. 7). The ossification proceeds rather rapidly as is well seen in a 4 to 4 1/2 month (11 cm.) embryo. The early centers of ossification which come to lie dorsally and ventrally do not correspond with the centers of chondrification of the cartilaginous stage the latter being situated early to the left and right of the ventrodorsal extension of

the perichordal sheath. The dorsal blood lake and center of ossification enlarges more rapidly displacing the still remaining mucoid streak ventrally. Soon the anterior and posterior centers fuse and form one large center of ossification. The first centers appear in the lower thoracic and upper lumbar region and rapidly extend cranially but less rapidly caudally. The central bone nucleus gives off capillary vessels which are resorbing the cartilage all around it in a star shaped manner. The mucoid streak normally is destroyed by this process, but occasionally remnants will remain. At about the twenty-second to twenty-fourth week of fetal life the ossification center has divided the cartilaginous body completely into two thick cartilaginous plates which show endochondral ossification toward the intervertebral disk. At the site of entrance of the vertebral vessels anteriorly and posteriorly large funnel shaped osseous channels form which, in sagittal sections, appear as bony triangles (Fig. 6). Small osteomas may be formed in these locations. No true cortical bone is seen. Along the anterior and lateral periphery the cartilage plates form horseshoe-shaped structures overhanging the cancellous portion of the vertebral body. It appears wedge shaped on sagittal section and it represents the cartilaginous ring epiphysis. It will form at a much later stage in young adolescent life the anlage for the true bony ring epiphyses (rim ledge) or the *Hafteepiphyse* of Schmorl. The cartilaginous



Fig 13



Fig 14



Fig 15

Fig 13 R van P, Hospital No 38-25,409, male, age, 29 years, has partial and complete fusion of 10th, 11th, and 12th dorsal vertebrae and fusion of the anterior margins of the bodies of the 8th and 9th dorsal vertebrae.

Fig 14 Ch A., Hospital No B-2464, male, age, 17 years, presents synostosis of 2d and 3d cervical vertebrae posteriorly. Failure of fusion of anterior and posterior ossification centers of 2d and 3d cervical vertebrae. Posterior displacement with wedging of the posterior fused portion. Patient had symptoms of slowly progressing cord compression.

Fig 15 Th. D, male, age, 8 years. Hospital No D 3895. Congenital scoliosis. Unilateral wedge vertebra between 6th and 7th dorsal vertebrae.

Fig 16 Bilateral half vertebrae involving 3d and 4th dorsal vertebrae, in a stillborn, full term infant. No wedging present.

Fig 17 L J, Hospital No 42-3116 male, age, 22 years. Posterior half vertebra—2d lumbar with wedging.



Fig 16



Fig 17

ring is the site of insertion of some of the fibers of the anterior and lateral annulus fibrosus, and they will be firmly incorporated as Sharpey's fibers at the time of ossification. No such arrangement is present along the posterior portions of the annulus fibrosus and the posterior margin of the cartilaginous plate.

The understanding of the blood supply and its fate is of special importance for the later understanding of the development of the intervertebral disc. The explanation of some of the nuclear prolapses into the spongiosa of the vertebral bodies occurring at an age when the senescent degenerative changes of the carti-



Fig. 8. Anterop. Va. A 41-35. Notochordal tissue remnant, N.C.R., spreading along the brain stem, BS. In woman who died of carcinoma of the lung. Microscopically the tissue is identical in appearance with that of chordoma. OC Optic chiasm.

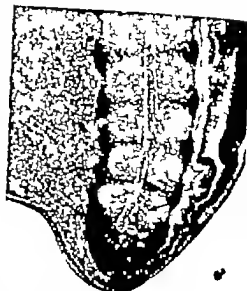


Fig. 10. Seven week (7 cm) embryo. Showing misplaced notochordal crisis in tail end of spine (arrow).

laminous plates are only minimal can be based on it. The intervertebral disc is constantly exposed to more or less severe trauma and it is one of the earliest structures to show definite senescent changes. This is partly explainable on the development and the early regression of the vascular supply. In addition to the articular vessels which parallel the notochord, as early as 3 1/2 months (9 cm.) other vessels are derived from the periosteum and penetrate into the cartilaginous plates without entering the central zone of ossification of the vertebral bodies. Uebermuth showed that these vessels enter the intervertebral cartilage at regular intervals all along the rim of the vertebral body and run in the direction of the nucleus pulposus. Those radially placed vessels are responsible for the toothed appearance of the epiphyseal plates of the growing vertebrae and the deep indentation seen in the bony vertebral bodies of the young growing child. Zones of calcification and the numerous foci of ossification develop along these vessels and free to form the ring epiphysis. Other vessels coming from the vertebral body penetrate the cartilaginous plates directly forming anastomotic arcades with those coming from the periosteum (Figs. 7 and 8). A moderate

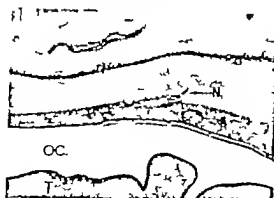


Fig. 9. Seven week (6 cm) embryo. Showing exit of notochord from the basilar cartilage (N) approaching the pharyngeal masses. Notochord situated partly outside of the cartilaginous tissue. OC Oral cavity T tongue, at left, anterior; at right, posterior.

amount of connective tissue accompanies the vessels into the cartilage. These vascular structures in the cartilage are well seen in embryonic life. Regression and scarring starts shortly after birth and slowly progresses to completeness by the age of 18 to 25 years, at which time most of the growth has stopped and the bony ring epiphysis has fused with the vertebral bodies proper. Where those vessels have penetrated the cartilaginous plates some chondrification gaps result. These are replaced at the time of complete degeneration of the vessels by either cartilaginous plugs or by scar tissue and sometimes by calcification. They form areas of lessened resistance to the increased turgor of the semisolid intervertebral disc substance especially if the disc is subjected to increased pressure. Through these points of reduced resistance nuclear prolapses occur, forming the so called Schorml's nodes (Fig 9).

Even in the embryo and the very young child at times when the intervertebral disc shows an excellent vascular supply, there is no direct vascular supply to the nucleus pulposus embedded within the annulus. Only the outermost zone of the annulus receives capillary vessels. However, Uebermuth described some brushlike vascular endings which enter this avascular zone. They are supposed to be derived from the previously described vessels.

All of these vessels degenerate gradually, and at 25 years of age none of them remains and the intervertebral disc becomes truly avascular. The only nutrition to the disc following this time is by diffusion processes through the cartilaginous plates coming from the cancellous vertebral bodies. Following this the intervertebral disc is slowly replaced by fibrous and cartilaginous tissue losing its turgor. The maximal turgor and elasticity are present about the 25th and 30th years of life. They decrease more or less rapidly after that time depending on the water content of the disc and annulus. The fate of the nucleus pulposus is also of importance since it forms the noncompressible semifluid medium which is so all important for the proper distribution of the pressure forces over the weight bearing surfaces of the vertebral bodies. Soon after the notochordal cells have all been squeezed

into the region of the disc, the cells undergo mucoid degenerative changes and some authors even state that they proliferate. They become clumped together forming a syncytium surrounded by mucoid material. This mass of material is increased soon by the addition of fibrous tissue and hyaline cartilage cells (Fig 8). Some authors describe fibrocartilage. The notochordal cells can often be demonstrated until adolescent life and older. After the disc becomes completely avascular during the third decade the nucleus pulposus slowly becomes replaced by fibrous tissue and loses the normal semifluid consistency. No vessels enter this structure except those which may penetrate into a severely degenerated disc during repair processes.

The annulus fibrosus, early, shows no evidence of collagen fiber deposition. In a 4 month (11 cm) old embryo, definite intercellular fibers can be seen all along the periphery of the disc. In a 5½ month (19 cm) old embryo, the fibers are very well developed and the appearance of the annulus in this stage is that of fibrocartilage. Weigert elastic tissue stains showed no elastic tissue fibers within the annulus during the embryonic life or in an 18 month old child, this differs from the findings of some investigators (4, 13).

Clinically there is evidence (24) that the annulus fibrosus has some nerve supply, but until recent years this has been denied. Jung and Brunschwig (14) demonstrated the presence of nerve fibers histologically beneath the anterior longitudinal ligament (Fig 10). Recently Rooft showed that some are also present beneath the posterior ligamentous structures (Fig 11). Sections through a 5½ month embryo stained with the Bodian technique show the presence of large nerve bundles beneath the posterior longitudinal ligament as well as within the annulus fibrosus proper. Nerve fibers beneath the anterior ligament give off fine branches which accompany the periosteal vessels entering the cartilaginous disc substance (Fig 12). The derivation and the type of these nerves is not clear. Rooft and, earlier, Luschka (*nervus sinuvertebralis*) state that the posterior bundles are derived from a recurrent branch just distal to the posterior root ganglion. This nerve, after sep-

arating from the main trunk, re-enters the intervertebral foramen and supplies the ligamentous structures two vertebrae lower than the exit of the spinal nerve.

Developmental defects of the spinal column have been poorly understood. One has to differentiate between the malformations occurring in the vertebrae intervertebral discs column and those along the neural column formed by the neural arches. The latter malformations have a close relationship with developmental defects of the neural tube (6 7 8 9).

Putti at a rather early date attempted to explain many of the defects on the basis of the mesenchymal and cartilaginous state of embryonic development. However many of his conclusions were based on animal observations which do not correspond with the embryology in the human. Junghans (15 16) has given a very excellent summary which contains some very good schematic drawings and explanations. Not all the developmental defects in the vertebrae-disc column can be explained on the basis of malformations in the mesenchymal and cartilaginous embryonic states. Many however become very easily understandable if one considers the vascular supply and the changes which occur in the notochord during the different stages.

**Congenital synostosis (block vertebrae)** There is complete or partial congenital bony fusion of two or more vertebral bodies without evidence of any or only small amounts of interposed intervertebral disc tissue (Figs. 13 and 14). This may be on the basis of complete chondrification of the dense mesenchymal zone which would normally form the annulus fibrosus. The cartilage bodies of the preosseous vertebrae fuse and they become ossified in one mass after the perinotal vessels penetrate into the cartilage. This malformation is then on the basis of a complete regression of the primitive annulus fibrosus.

**Sagittal cleft vertebrae** Persistence of the ventrodorsal extension (10 11 23) of the perichordal sheath with or without the persistence of the chorda or splitting of the notochord (6 7 8 9) in this area may prevent fusion of the laterally situated cartilaginous vertebral halves. Each half may become ossified separately by its anterior and posterior centers with

persistence of the sagittal cleft. With weight bearing in later life such vertebrae may form the butterfly vertebral bodies.

**Lateral half vertebrae or wedge vertebrae** At times only single lateral half vertebrae are seen (Fig. 15). Feller and Sternberg (6 7 8 9) believe that they have their origin in the cartilaginous state of the embryonic life and they have observed that the chorda shows a curvature toward the side of the half vertebrae with absence of cartilaginous development on the other. Junghans and others (17) believe that the origin of the half vertebrae is on the basis of lack of blood supply to the missing half of the body. At first these half vertebrae are cuboidal in shape but they become a wedge as soon as weight bearing occurs. Bilaterally occurring half vertebrae may involve large segments of the spinal column as wedged hemivertebrae at different levels (Fig. 16). They are placed one on each side and will give in later life a bilateral bony scoliotic curve. They are most commonly explained on the faulty unilateral cranial hemimetameric shift of the vertebral segments which occurs in the blastemic period. Thus unilateral occurring shift will cause an anlage for a half vertebra to remain at the lower and the upper end of the unequally shifted column which will later undergo chondrification and ossification.

**Ventral and dorsal half vertebrae** These are rare (Fig. 17). The explanation for these must be on the basis of faulty vascularization and agenesis of either the anterior or posterior center of ossification. They fuse normally rarely. The rôle of the notochord in these cases is not quite clear. Feller and Sternberg believe that the notochord is missing in these places. It is logical to assume that the lack of vascularization of either the anterior or the posterior portion will cause either one of them to remain in a cartilaginous state. The malformed vertebral bodies will at times take the form of wedges as soon as weight bearing is started. The deformity resulting will be of the gibbous type.

**Malformations of the chorda and chordal remnants** During the state of migration of the notochordal cells during the cartilaginous period of embryonic development, there is definite persistence of the perichordal sheath form-

ing the mucoid streak. Anywhere along the course of this structure which normally regresses completely during the ossification of the vertebral bodies, chordal cell remnants may be found (Fig 3). These remnants have been found and reported nearly everywhere in the spinal column. One of the more frequent abnormalities seen are the outpouchings of the otherwise normal intervertebral discs which is usually associated with thinning of the cartilage plate in the zones where the mucoid streak entered the intervertebral disc. Those weakened places are often the site of centrally placed nuclear prolapses into the adjoining vertebral bodies. Sometimes true extensions of the nuclear material in a wedge-like manner can be seen protruding into the vertebra. A few cases have been reported in which the complete chorda has persisted as a solid central mass connecting two or more intervertebral discs.

During postmortem examinations notochordal tissue remnants are present in 2 per cent of the cases. Most of these are found in the region of the clivus at the base of the skull (Fig 18). The notochordal cells during the normal development are doomed to undergo degeneration if they remain enclosed within cartilaginous or fibrocartilaginous tissue. This is obviously the case in the normal intervertebral disc and no notochordal cells are seen after the late adolescent period. In certain areas as in the notochordal extension within the base of the skull and in the sacrococcygeal region only a moderate amount of cartilaginous tissue will surround the chorda. In a few places the notochord normally is situated outside of dense mesenchymal or cartilaginous regions during the embryologic development. This is the case at the roof of the oral cavity where the chorda enters into close relationship with the lining pharyngeal mucosa (Fig 19). It also comes to lie rather free just posterior to the hypophyseal pouch. Another area is close to the foramen magnum and the odontoid process. The same is true in the region of the rather undifferentiated tail end of the spinal column where only very rudimentary vertebrae are formed by the mesenchymal tissue and the cartilaginous and ossification processes (Fig 20). In these areas some blood

supply may be retained and the notochordal cells fail to degenerate. These are the locations where in adult life most chordomas occur. Occasionally they have been reported along the spinal column. The latter can be explained on the basis of remnants included in the vertebral bodies where the blood supply is maintained.

*Congenital weaknesses of the cartilage plates*  
In areas where the cartilage plates are penetrated by vessels from the vertebrae, mostly along the peripheral two-thirds and in the center where the axial vessels accompany the notochord, chondrification gaps develop (Figs 7 and 8). These are evident in the embryonic sections and in sections through the adolescent intervertebral discs. These areas form points of lessened resistance to the increased turgor of the nuclear material and at times, the latter will be forced through these gaps to form spongiosal prolapses (Fig 9). If this occurs during the actively growing state of the adolescent period the process will be a rather gradual one stimulating considerable cartilage formation, but little reactive bone. Thus, often no reactive bony cup can be seen early in the x-ray pictures. Also, no true tears of the cartilage plate will result. In older persons after the growth period has ended, the prolapsing material is more of a fibrous nature and the reparative process proceeds rapidly to reactive bone and a bony cup becomes visible in x-ray pictures.

Multiple spongiosal nuclear prolapses with juvenile kyphosis in the young adolescent groups occur mostly in boys subjected to very heavy manual labor. One must keep in mind that at this age there is still good blood supply to the intervertebral disc tissue and not all the vessels have degenerated. The nucleus pulposus is still rather liquid and easily displaced. Scheuermann, basing his observations and this theory only on x-ray findings, states that the deformity is due to an aseptic necrosis—an "epiphysitis" of the ring epiphysis which is undergoing marked ossification at about this age. Schmorl and since then others (22) have examined, at autopsies, numerous spines of adolescent patients with juvenile kyphosis, and they found large nuclear prolapses into the spongiosa through the cartilage plates. These prolapses are in a location which is



usually the one where some of the chondrification gaps have occurred due to degenerated vessels producing weak points. It also has been proved fairly conclusively that the ring epiphysis has nothing to do with the growth in the height of the vertebral bodies. This growth in the height is exclusively a function of the cartilage plate which is central to the ring epiphysis and underlies the rim ledge proper. Nuclear prolapses of juvenile kyphosis often occur all along the vertebral bodies of the lower thoracic and upper lumbar region. The uneven growth in height of individual vertebrae tends to retard the growth anteriorly where the increased pressure load is concentrated. More normal growth occurs posteriorly. Thus, the relative wedging of the vertebral bodies is secondary to the improper mechanical function of the degenerating narrowed intervertebral disc. In this way the kyphotic deformity results. The fragmentation of the anterior portion of the ring epiphysis seen in x ray pictures results from improper motion, abnormal pressure relationship and shearing stress put upon the anterior annulus fibers and the unfused ring epiphysis.

#### SUMMARY

An attempt has been made to describe and illustrate the development of the vertebrae

and the intervertebral discs, and to correlate developmental peculiarities with certain lesions found in later life.

#### REFERENCES

1. BODIAN, D. *Anat. Rec.*, 1935, 64, 81
2. BORDANO, R. *Arch. Klin. Chir.* 1938, 51, 52
3. IDEM. *Verh. Arch.*, 93, 280, 8, 3
4. BRADFORD, P. K. and SUTCLIFFE, R. G. The Intervertebral Disc. Baltimore: C. C. Thomas, 40
5. CALVE, J. and GALLAGHER, M. J. *Bone* 1937, 14, 335
6. FELLNER, A. and STRECKENBACH, H. *Verh. Ges. orth. 87, 63*
7. *Ibid.*, 930, 578, 666
8. *Ibid.*, 931, 287, 449
9. *Ibid.*, 932, 285
10. HANCOCK, R. *Acta chir. scand.* 1931, 66, 303
11. HANCKENSTADT, R. J. *Zentr. orthop. Chir.* 1935, 11, 332
12. HODGINS, J. T. FRANKS, C. H. *Burg. Gyn. Obst.* 1902, 7, 796
13. HOLMAN, W. L., DUFF, G. L. *Am. J. M. Sc.* 1918, 98, 46
14. JUNG, A., STRECKENBACH, A. *Fortschr.* 1913, 174
15. JOCHIMANN, H. *Heute-Lebende, Handb. der spec. path. Anat. und Hist.* Vol. 9, 4. Reihe, 1. Jg. J. Springer, 939
16. IDEM. *Arch. orthop. Unfallchir.*, 937, 23
17. NALLIED, T. *Ber. Klin. Chir.* 1896, 95, 21
18. PETER, V. *Fortschr. Röntgenstrahl.*, 1929, 14, 25
19. ROORE, P. G. *Arch. New Psychol.* 1928, 47, 109
20. SCHREIBER, H. *Zentr. orthop. Chir.* 1931, 7, 275
21. SCHWARTZ, G. *Klin. Woch.*, 1929, 7, 243
22. IDEM. *Fortschr. Röntgenstrahl.*, 1930, 4, 179
23. SCHWARTZ, M. *Fortschr. Röntgenstrahl.* 1937, 16, 253
24. SEVERINO, G. GRANTHAM, E. *Arch. Surg.* 1947, 47, 375
25. STRECKENBACH, H. *Arch. Klin. Chir.* 1939, 51, 87

# MESONEPHROMA OR TERATOID ADENOCYSTOMA OF THE OVARY

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THE etiological relationship between the various residual elements of the wolffian body which survive in the adult and gynecological neoplasms has always been an interesting one. The origin of certain cysts and tumors from the remnants of the wolffian duct system has been generally accepted but until Schiller (16) in 1939 described a semisolid ovarian tumor of the ovary and postulated the mesonephros as providing the background for its development, the wolffian body itself has not been seriously considered as a source of ovarian neoplasms. There seems to be no theoretical reason why mesonephric tumors should not develop in the ovary or the tissue adjacent to it particularly as tumors of adrenal cortical cells of the ovary and mesovarium are well recognized. In fact, it would seem more difficult to explain why tumors of the wolffian tubular system are not the source of neoplastic phenomena in the ovary. Such tumors in retroperitoneal regions are well known and their morphological characteristics as well as their mode of growth and life histories have been described in considerable detail. The question raised by Schiller is therefore one of great interest, and additional information is needed in order to prove or disprove the thesis which he has proposed.

Although 3 years have elapsed since the original contribution only a few papers have appeared upon the subject, notably those of Jones and Seegar (7, 8), Kazancigil, Laquer and Ladewig (11), Tuta and Siebel, and that of Rosenblatt and Grayzel. In all, 30 instances of so called "mesonephroma ovarii" have been studied and reported which appear, at least in part, to fulfill the criteria outlined by Schiller. We wish to report 10 more ovarian tumors which seem to us to fall into this category.

A study of the previous reports upon this subject indicates that although nearly all writers agree that a characteristic tumor of the ovary has been described having a characteristic morphology in many respects, which for the time being should justify its being placed in a special category, there are reservations as to its etiological relationship to the mesonephros. Jones and Seegar state that "the theory of the mesonephric origin of these tumors, while plausible is not yet proven." Their skepticism is based largely upon the absence of "glomerular" bodies in the tumors studied by them. They come to this conclusion although the general structure of the tumors was in other respects remarkably similar to those of Schiller's report. Kazancigil and co-workers report a study in which they made serial sections through glomerulus-like structures, without finding anything that resembled a vascular tuft. Such an observation, although not necessarily conclusive, is to us significant. On the other hand, the failure to demonstrate a structure so highly differentiated as a glomerular capillary bed in a neoplasm cannot be considered as final proof that there is no relationship to the mesonephric organ.

In our series of tumors we have usually been at a loss to demonstrate structures which even remotely resembled the architectural arrangement of wolffian glomeruli. It is true that the tumors abounded in acini into which papillary tufts of epithelium projected with or without a supporting connective tissue stalk, but one would be as justified in naming any one of several well recognized ovarian or uterine tumors as "mesonephric" if the demonstration of this arrangement of cells were to be taken as the criteria of such origin.

Retroperitoneal wolffian tumors on the contrary, such as have been described by many writers, are characterized by much more definite glomerulus-like structures. The literature

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goes back to 1894 when Frank reported his studies. Hinman, Gibson and Kutzmann in 1924 and more recently Hardeman and De Groot have all emphasized the point that "one definite criterion of mesonephric origin is the presence of the primitive glomeruli or renal tubules.

Although most of the ovarian tumors reported have been characterized by closely packed acini lined by low cuboidal epithelium which could easily be interpreted as a formation of wolffian tubules the infrequency or dearth of the "glomerular" structures is significant. It is difficult to believe that the ovary offers an environment so different from the retroperitoneum as to produce a relative lack in glomerulus formation while allowing at the same time a profuse growth of ducts.

We are skeptical therefore, of Schiller's explanation of the etiology of this group of tumors and prefer not to accept his term, mesonephroma ovarii, for them. We are on the other hand convinced that they are not rare that they form a morphologically distinct group of ovarian tumors with a characteristic life history and that they should for this reason have a distinctive name and more important that they should be studied as such so that more can be learned about them.

We are at variance with those who have expressed the belief that these tumors are merely a hydrotic form of serous cystadenoma, for these tumors almost invariably produce a mucin-like substance which reacts to the usual stains for mucin. While the mucin stain is non-specific, the fact that it is positive in these tumors serves to differentiate it from the serous group in which it is not positive. At the same time this finding indicates a probable relationship to wolffian or teratoid antecedents. On the other hand these neoplasms are quite different morphologically from the pseudomucinous cystadenomas, as well as different in their mode of growth. Whether benign or malignant they are essentially solid tumors which tend to become cystic only as they degenerate.

#### CASE REPORTS

CASE I Miss A. S. N. 33, 5, cut of age single, was admitted to the New York Hospital on

October 4, 1937 complaining of suprapubic pain and dull ache pain on the inner aspect of the right thigh and feeling of something rubbing on the inside of the abdomen. These symptoms had been present 16 months. She had had no postmenopausal bleeding since uncomplicated menopause 7 years previous. Examination revealed a movable and nontender abdominal mass arising from the left pelvis and extending up to two fingerbreadths below the umbilicus. On October 6, 1937 a subtotal hysterectomy, right salpingo-oophorectomy and a left salpingo-oophorectomy were performed. The large cystic left ovary, right ovary broad ligament and omentum were involved in tumor tissue. The patient received postoperative radiation before discharge from the hospital. Within 6 months, the patient was in hopeless state with extensive recurrence of the tumor.

**Pathology.** The tumor tissue consisted of papillary and cystic structures with infiltrating growth. The left ovarian cyst measured 15 by 11 by 8 centimeters, the lower pole of which was papillary and semisolid. Microscopically the tumor tissue was lobulated, encapsulated, and supported on a fibrous connective tissue framework. In some areas solid sheets, clumps here and there, and a tendency toward a fairly typical and high cellular arrangement prevailed. Fibrous papillary processes containing nests of the typical acini were also seen, the acini as in the other tumors had below contained mucin like material. The individual cells were of fairly uniform pattern not markedly basophilic and were arranged in a single, though at times crowded, row. Nuclei were open, pleomorphic and clearly delineated. Occasional mitoses were seen in one section (Fig. 3) there were resemblances to papillary serous cystadenoma.

CASE 2 Miss R. W. N. 297 43 years of age, primipara, hit with a normal menstrual history, complained, on admission to the New York Hospital on November 7, 1937 of a enlarging lump in her abdomen which had been present for 6 months. There was associated fatigue and a 10 pound weight loss. Examination revealed a mass arising in the pelvis and extending to the umbilicus. It was nontender, no tender and nodular. At operation, 6 days later, the large ovarian tumor together with both tubes, right ovary and fundus of the uterus were removed. There was no evidence of metastasis. She received postoperative radiation. She is to date in good health and has no evidence of recurrence.

**Pathology.** The uterus, right tube and ovary appeared normal. The left tube stretched over as encapsulated ovarian tumor measuring 11 by 10 centimeters. On section the semisolid tumor in its central portion was of gelatinous character. The outer 1 was made up of solid cords of yellowish elastic tissue. Microscopically within fibrous capsules a fibrovascular stromal background were nests, clusters, and sheets of epithelial elements. Although the histologic features resemble structures of Schiller tumors are readily found there was a tendency toward

luteinization so much so as in some areas to simulate granulosa cell tumor of the Lecene type (Fig 4)

CASE 3 Miss M A, No 245875, 19 years of age, Italian, was first admitted to the New York Hospital on September 21, 1939, with an enlarging abdominal tumor of 4 months' duration, suspected by the patient as being due to pregnancy. Examination disclosed a firm, cystic, and smooth mobile tumor filling the cul-de-sac and extending into the abdomen. At operation 5 days later considerable free fluid was found in the abdomen, the left ovarian cyst and tube were removed. She remained free of symptoms until one week prior to her second admission (May 12, 1940) at which time there developed pain and swelling of the abdomen. A right adnexal semicystic mass was noted to extend from the cul-de-sac to the umbilicus. The following morning, a laparotomy was performed. Extensive tumor involvement was noted, only part of which could be removed. The patient died poorly thereafter and died on July 19, 1940. Autopsy permission was not granted.

*Pathology* The original specimen consisted of a collapsed thin walled and multilocular cyst measuring 10 by 16 by 12 centimeters. The internal surface had many elevated solid areas, some of which were infiltrated with hemorrhage. Gross material from the second operation was very soft, loosely organized, and friable. Mucin-like material exuded from the cut surface. Microscopically, the appearance was of a loose and irregular arrangement of the delicate epithelial cells, with some tendency toward acinar and gland like formations. Mitoses were not infrequent. There was little stromal tissue and this was of varying density. Considerable necrosis and degeneration were noted in some areas.

CASE 4 Mrs M S, No 24048, 64 years of age, was admitted to the New York Hospital on June 20, 1940, because of swelling of the abdomen, ascites, and abdominopelvic tumor. Eleven months previously a lower abdominal tumor was incidentally found during a hernioplasty. Follow-up at that time was refused by the patient. On June 26, at operation, a large adherent left pelvic tumor together with the left tube and ovary was removed. Liver metastasis were noted at that time. Following discharge, her course was slowly downhill. She was readmitted on November 11, 1940, and died 5 days later. Autopsy revealed widespread tumor involvement of peritoneal cavity and metastases including involvement of liver, bowel, spleen, and pleura.

*Pathology* The operative specimen was a multilocular semisolid ovarian cyst with penetrating tumor tissue, measuring 16 by 13 by 10 centimeters. On section, papillary neoplastic tissues were found in several loculi. Throughout the microscopic pattern was quite characteristic. The typical epithelium lined cysts and acini varied greatly in size. Some contained considerable epithelial elements and appeared superficially as glomeruli. Careful examination did not bear this out. A fibrous background was present and in a few areas there was some evidence of tendency toward papillary serous cystadenoma.

CASE 5 Miss H S, No 291061, 68 years of age, was known to have an abdominal tumor for 2½ years, prior to her first admission to the New York Hospital on March 25, 1941. More recently she had complained of pain in the lower abdomen and groin, and of a 25 pound weight loss. Examination revealed ascites and a large cystic mass filling the lower abdomen and pelvis. At operation 2 days later the large left ovarian tumor together with the right ovary, both tubes and fundus of the uterus was removed. Pelvic implants were noted. Postoperative x-ray therapy was given. Recurrence was evident 7 months later, and in November she was readmitted in a cachectic state. At that time a right lower quadrant abdominal tumor was palpable. The patient was discharged temporarily improved after a 2 weeks' hospital stay.

*Pathology* The tumor measured 12 by 17 by 20 centimeters. At one pole the capsule was penetrated by a friable, solid mass. On section, a large cyst filled with thick dark brown material was noted, elsewhere the tumor was solid. Microscopically, the tissue was highly cellular with sheets of delicate epithelial cells. In some areas there was an attempt at acinar formation. Elsewhere it was less differentiated and in these, where cells were closely packed, the cytoplasm appeared clear due to hydropic degeneration. The adenomatous areas were typical (Fig 2), and served to classify this tumor with the "mesonephric" group.

CASE 6 Miss J B, No 25123, 52 years of age, a nurse, was admitted to the New York Hospital on April 9, 1941, because of symptoms of intermittent groin pains of 5 months' duration, and with the finding of a moderately tender, firm, round mass the size of an orange in the left pelvis. At operation 5 days later a left broad ligament cyst together with the left ovary, fundus of the uterus, and appendix, was removed. Postoperative radiation was given. When last seen 7 months later, the patient was in good health and there was no evidence of recurrence.

*Pathology* The collapsed cyst must have measured 7 centimeters in diameter. It was lined with cake-like projecting masses which on section were found composed of yellowish material. No tumor tissue was found in the other specimens. Microscopically, the tissue consisted largely and quite uniformly of typical cells. They were arranged in nests and acini separated by thin fibrous septa. The whole tumor was well differentiated.

CASE 7 Mrs B S, No 6557, 51 years of age. Because of a known myomatous uterus this patient had been followed carefully since 1933. A large abdominopelvic tumor extending to the umbilicus was first found at her regular 6 months visit in April 1941. She complained, on admission to the New York Hospital, of pressure symptoms of 1 month's duration. At operation on May 6, 1941, the large left cystic ovarian mass and myomatous uterus, together with both tubes and right ovary were removed. Her postoperative course was uneventful and she is to date free of evidence of recurrence.

**Pathology** The semisolid ovarian cyst measured 8 by 9 by 1 centimeters. No penetrating growth was evident. On section, the multilocular cyst contained gelatinous material. Its center was solid. The uterus contained several myomas. The other specimens were not remarkable. Microscopically there was an extensive fibrous and hyaline supporting tissue. Scattered through this were aggregated nests of epithelial structures, some of which had an alveolar pattern. Papillomatous areas were also present which, like those of Case 4, simulated serous cysts. However, material in acini and inter papillary spaces was found which responded to mucin stains.

**CASE 5.** Mrs. E. A., No. 60696, 30 years of age, on admission to the New York Hospital on July 3, 1942 gave a history of a noticeable enlargement of the abdomen associated with some recent right lower quadrant abdominal pain for the last 6 months. Examination revealed a large cystic mass arising in the pelvis and extending to the xiphoid. Two days later at operation the large cystic right ovary together with both tubes, left ovary and uterus was removed. No extension or implants were found. She received postoperative radiation and was discharged apparently well.

**Pathology** On gross examination the cyst was found to be unilocular, about 30 centimeters in diameter. The wall contained several papillary areas, many degenerative. Microscopic sections of several areas showed the typical pattern with clusters, papillary and alveolar groupings of epithelium-like cells. The larger clefts and spaces contained debris and a precipitated mucinous material. Considerable degeneration was also present.

**CASE 6.** Mrs. M. W., 48 years of age, complained of pain in the right lower quadrant of the abdomen for months. A tender mass of centimeters in diameter was found. At operation on November 17, 1944 a subtotal hysterectomy, right salpingo-oophorectomy, left salpingo-oophorectomy and appendectomy were performed.

**Pathology** The thin walled multilocular ovarian cyst weighed 358 grams and contained clear and mucinous material. In the larger cyst a irregular mass, 3 by 3 centimeters projected. The other specimens were not remarkable. Microscopically sheets and clusters of epithelial cells, in some areas with clear cytoplasm like those in histiocytic granulosa cell tumors, were found. There were scattered divisional fibrous septa. Elsewhere areas were present in the sections which were clearly recognized as thecoma. However in other parts, a characteristic arrangement of the cells typical of the so called mesenchymal tumor was seen and served to classify by this with the group. Considerable necrosis was spread throughout the several fields.

**CASE 7.** Baby S, months old, because of vaginal bleeding for 3 months, was examined by gynecologist and biopsy specimen of glandular form

tumor was taken. Extensive radiation was given notwithstanding, vaginal bleeding recurred 3 months later and examination disclosed recurrence. Radiation was repeated but without effect. The infant died at age 18 months, December 30, 1947. Autopsy revealed extensive pelvic mass metastatic to lungs and mediastinum.

**Pathology** Under low power magnification, there was less resemblance to the classical picture in these scattered small nests and acini of epithelial cells in a fibrous background. However on careful scrutiny under high power, the epithelial cells were typical and found to line the acini in the characteristic crowded single and multiflayered fashion. Necrosis and degeneration was extensive.

#### GENERAL DESCRIPTION OF THE TUMORS

The tumors occurred in the left ovary in 15 but 2 instances. The ages of the patients ranged from 11 months to 68 years; one was an infant, another was 19 years, and all the rest were over 30 with the oldest 63 years.

Usually the growth is oval in shape measuring from 3 to 17 centimeters in the smallest diameter. The capsule is ordinarily varied in thickness being thin and bosselated over the cystic areas and more dense over the solid portions. Occasionally papillary processes penetrate the capsule and appear on the external surface. However generally the external surface is smooth and free of growth or adhesions.

The inner aspect of the tumors present multiple cysts of different sizes and a solid portion which is usually situated on one side of the cyst. In the solid portions are areas of recent growth which are pinkish-gray in color; elsewhere they are largely composed of rather old grayish-yellow tissue and often contain areas of degeneration. Fatty degeneration, as proved microscopically by fat stains, is not

**Fig. 1.** Camera lucida drawing (high power magnification) showing the characteristic solid inner structure of teratoid adenocarcinoma. Note the typical hydrophilic epithelial lining cells, arranged in single and multiflayered manner.

**Fig. 2.** Photomicrograph of well differentiated tumor showing alveolar like single layered epithelial lining. Several intra-alveolar spaces contain mucoid material (Hematoxylin and eosin stain. X 100).

**Fig. 3.** Photomicrograph of papillomatous area, showing papillae covered by typical epithelium (Hematoxylin and eosin stain. X 100).

**Fig. 4.** Photomicrograph of an undifferentiated tumor. Laminar cells are closely packed in sheets, separated by thin fibrous septa. Note the light staining cytoplasm of the older cells (Hematoxylin and eosin stain. X 100).

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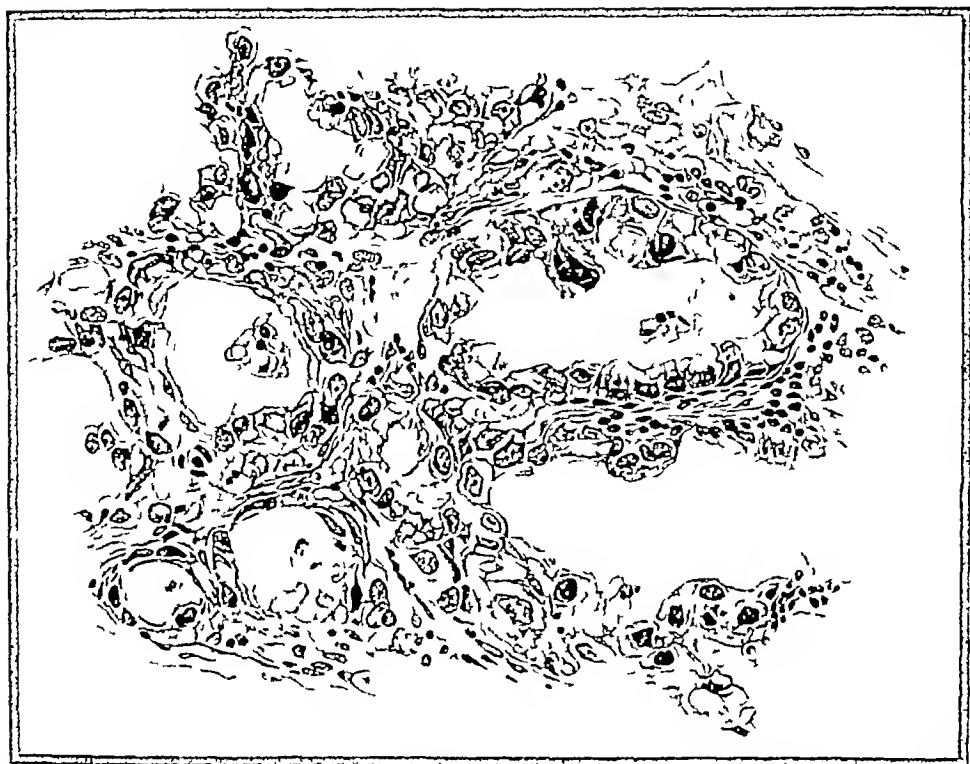


Fig 1



Fig 2



Fig 3



Fig 4



TABLE I—SUMMARY OF TEN CASES REPORTED

Case number	History number	Age	Symptoms	Clinical findings	Operative findings	Primary site	Treatment	Result
1	182234	50	Suprapubic pain pain inner aspect right thigh 6 mos	Abdominopelvic mass rising to two fingers below the umbilicus	Adherent papillary and semisolid cyst with penetration and metas- tases	Left	Operation	Recurrence 3 mos
	102207	43	Mass in the abdomen 6 mos Weight loss and fatigue	Abdominopelvic mass extending to the um- bilicus	Encapsulated tumor 12x 12x16 cm Semi-solid	Left	Operation and x ray	No recur- rence 4 yrs.
3	245875	19	Enlarging of abdo- men left lower quadrant pain 4 mos.	Cystic tumor from cul-de- sac to the umbilicus ascites	Ruptured cyst 10x10x12 cm thin walled multi- locular and hemorrhagic	Left	Operation	Died in 10 mos.
4	24048	64	Swelling of abdomen 3 wks Swelling of left groin legs anorexia	Large firm abdomino- pelvic tumor Ascites	Semisolid cyst 16x13x10 cm with papillary pen- etration, ascites. Au- topsy Widespread in- volvement with distant metastases	Left	Operation	Died in 5 mos.
5	291061	68	(1) Abdominal tumor 2½ yrs Pain groin and abdomen 3 mos. Weight loss (2) Nausea vomit- ing constipation	(1) Cystic mass filling lower abdomen and pel- vis (2) Recurrent tumor on right, Bowel obstruction	Semisolid tumor 1 x 17x 20 cm Penetrating irri- table tissue Pelvic implants	Left	Operation and x ray	Recurrence in 7 mos.
6	25123	52	Intermittent groin pains of 5 mos.	Firm round mass left lower quadrant size of orange	Smooth walled cyst 7 cm in diameter	Left	Operation and x ray	No recur- rence 7 mos.
7	6557	51	Urinary frequency incontinence noc- turna dull lower abdominal ache 1 mo	Firm irregular fixed tumor from vaginal fornix to umbilicus	Multilocular semisolid cyst 8x9x10 cm No penetrating growth	Right	Operation	No recur- rence 5 mos.
8	60096	30	Enlargement of ab- domen and right lower quadrant pain 6 mos.	Large cystic mass filling pelvis and abdomen	Single cystic mass 20 cm in diameter	Right	Operation and x ray	Discharged well after 5 wks.
9	Gift	48	Pain right lower quadrant 2 mos	Tender mass of 10 cm diameter	Double cyst with no penetration	Left	Operation	?
10	Gift	11 mos	Vaginal bleeding 5 mos.	Vaginal fornix tumor	Autopsy revealed exten- sive pelvis masses with distant metastases	?	X ray	Died in 11 mos.

evidence with free fat in the intercellular and intra-alveolar spaces. Intracellular fat droplets are also seen in such locations. The cysts and cut surface of the solid portion of the tumor yield a shiny mucoid material, which is precipitated by both alcohol and acetic acid and stains in the tissues with thionin and mucicarmine.

The tumors probably are slow in rate of growth as our patients gave histories indicating the presence of the tumors from 6 months to 4 years.

Extension of the growth may be by implantation of papillary processes upon adjacent peritoneal structures followed by dissemination throughout the abdomen or the metastasis may be by way of the lymphatics. Free abdominal fluid is not a constant finding even when peritoneal involvement is present, however, it may occur. The omentum may be

the only abdominal structure containing gross metastases. However, extensive bowel implantation as well as nodules in the liver, spleen, and pleura were found.

#### MICROSCOPIC STRUCTURE

The larger cysts are usually lined by a single row of flattened cuboidal cells, while the smaller ones have a hydropic appearing epithelium in a single row, the cells being of varying heights depending upon their secretory activity.

The solid or semisolid tissues exhibit varying degrees of differentiation, the more adult types (Figs 1, 2) consisting of closely packed acini resembling tubules (collecting ducts?) lined by a single row of hydropic epithelium. Occasionally the acini contain papillary structures extending into them, consisting of one or more layers of columnar cells resting upon a



delicate connective tissue stalk. In the papillary tumors one can often demonstrate portions of the tumor in which large connective tissue structures are found lined by a single row of flattened epithelium resembling the serous type of growth seen in serous cystadenomas (Fig. 3). Doubtless it is this morphological variation which has led to the feeling in some quarters, that the so called "mesonephroma ovarii" is a type of serous tumor. With this view we cannot agree.

In less well differentiated tumors (Fig. 4) papillarity increases and the formation of acini decreases until in the least differentiated specimens the cells may lie in solid sheets.

The character of the epithelium is varied, depending upon age, secretory activity and degree of differentiation. The older epithelial cells may be quite low and having little cytoplasm may present a marked basophilic reaction. The young actively secretory cells, on the other hand, often are filled with fluid and have a very hydropic appearance. In this stage the product of secretion takes the usual mucin stains. When secretory cells are packed in close sheet formation the hydropic cytoplasm gives them an appearance resembling lutein or adrenal cortex cells. However they do not stain with Sudan III.

Our efforts to demonstrate glomerulus formation were not rewarded by the finding of convincing structures. Perhaps we expected too much in searching for something which looked like a simplified wolffian glomerulus. However we have been guided by the illustrations of wolffian tumors as reported by many writers, including Hinman, Gibson and Kutzmann.

The more malignant tumors as judged by the clinical course of the patient were those showing some papillary development and particularly those which were highly cellular and more completely undifferentiated.

It should be pointed out that from a morphological point of view these tumors can assume a variety of histological pictures and for this reason there will be those who will conclude that all of the tumors reported cannot have a common etiology. However a study of tissues taken from all portions of the tumors leads us to believe that the major portion of

them represents a common type of epithelial cell and that in general their variation in arrangement is such as might be expected as being due solely to variations in degree of differentiation.

One tumor however contained areas of undoubted theca and granulosa cells and another had areas which morphologically resembled the serous cystadenoma. Inasmuch as we believe that the so called "mesonephros" are in all probability teratoid cystadenomas the finding of cells of various types is not only to be expected on occasion but we should anticipate that as other studies of these tumors are reported they will become a much less clearly defined group of tumors. In our opinion, it is only the well differentiated type of tumor which closely stimulates the morphology as outlined by Schüller.

#### CLINICAL COURSE

Six of the 10 patients are dead or have extensive recurrence of the growth, indicating a high degree of malignancy. The other 4 patients have no recurrence thus far although it is too early to assume a sanguine attitude toward their future.

All of the patients received surgical treatment and 6 of these were given extensive post-operative x-ray radiation. Neither surgery nor the x-ray seems to have had any effect in prolonging the lives of the patients having the less differentiated type of tumor. A case is provided giving the main clinical and pathological characteristics.

#### SUMMARY AND CONCLUSIONS

This group of ovarian tumors has a distinct morphological background which, though subject to considerable variation, seems to differentiate them from other ovarian tumors. It would be a satisfaction if one could accept Schüller's theory of etiology. However the characteristic pseudoglomerulus is so frequently demonstrable that the linkage with the mesonephros is not possible. With what now known the similarity of the acini to collecting duct tubules is insufficient to make this relationship convincing. It is important, however for purposes of study as well as treatment to separate tumors into distinct categories.



# EXPERIMENTAL OBSERVATIONS ON RECONSTRUCTIVE INTRATHORACIC ESOPHAGOGASTRIC ANASTOMOSIS FOLLOWING RESECTION OF THE ESOPHAGUS FOR CARCINOMA

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CARCINOMA of the esophagus is rapidly assuming a more important position among the surgical entities. Thus recent progress has been demonstrated by the large number of successful transthoracic resections of carcinoma of the cardiac end of the stomach with re-establishment of the esophagogastric continuity which have been done. Until recently these patients were refused operation as being hopeless. This progress has been made possible by a more thorough understanding of the physiology of the thorax, the refinement of surgical technique and the progress that has been made in the field of anesthesia for major intrathoracic operations.

During the 10 year period between 1931 to 1941 at the University Hospital 185 patients have been seen with carcinoma of the esophagus. Approximately a quarter of the lesions in these cases occurred in each of the following situations, the upper one third, the middle one third, the lower one third of the esophagus, and carcinoma of the cardiac end of the stomach infiltrating the esophagus secondarily. Twenty five per cent of the patients with carcinoma of the esophagus coming to necropsy at the University Hospital had no evidence of metastases or extension of the carcinoma beyond the confines of the esophagus. Another 15 to 20 per cent had regional lymph node metastases alone. Consequently one might assume that approximately 40 per cent of the patients coming to necropsy present operable lesions. This compares with the reports by Abel who stated that 15 per cent of the fatal cases of carcinoma of the esophagus are oper-

able. Ochsmier and DeBakey presented a series of 1,015 patients with carcinoma of the esophagus observed at necropsy of whom 40.7 per cent showed no evidence of metastases. Sauerbruch found that 35 per cent of 117 patients in which the carcinoma was situated between the hilum and the cardia, died without forming distant metastases, and Starlinger found that 66 per cent of the cases examined had no metastases. Many patients die from either starvation perforation of the carcinoma with resulting mediastinitis and empyema, aspiration pneumonia or lung abscess.

The many obstacles in the progress of the surgical treatment of carcinoma of the esophagus have been stressed by Ochsmier and DeBakey. One of the chief obstacles is the inherent anatomical characteristics of the esophagus. The esophagus has no serosal covering upon which the success of gastrointestinal anastomosis depends. It has a very meager blood supply and consequently great care must be exercised in preserving all the blood supply to the remaining esophagus. The cuticular muscular coat is longitudinal and consequently tends to pull an anastomosis apart. The esophagus is relatively fixed and has no redundancy making operative procedures difficult. Furthermore carcinomas of the esophagus are located immediately adjacent to many vital structures, which make all operative procedures technically difficult. In addition to this anatomical background, patients with carcinoma of the esophagus usually present themselves in a dehydrated and malnourished or emaciated condition. They usually have avitaminoses with complications. Because of esophageal obstruction with stasis of food and mouth secretions, the bacterial flora are very virulent, and favor postoperative infections.

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Service.

Because, until recently, treatment of carcinoma of the esophagus has been so unsuccessful, the attention of the general practitioner has not been focused sharply enough upon the significance of dysphagia in the early diagnosis of this condition, and the importance of an early esophagoscopy examination has been widely neglected. It was shown in a comparative analysis of carcinoma of the gastrointestinal tract (5) that the smaller the caliber of the organ, the shorter the latent period, and the smaller the neoplasm before causing symptoms. The esophagus is a relatively small caliber organ and, therefore, a neoplasm should cause symptoms relatively early. Consequently, patients with carcinoma of the esophagus should present themselves for treatment much earlier than patients with carcinoma situated elsewhere in the gastrointestinal tract. Because of this, it is disheartening when patients present themselves with histories of dysphagia that has been present a year or longer. As surgical management improves, these patients will be referred for treatment earlier.

As to the disposal of the 185 patients with carcinoma of the esophagus seen in the last 10 years at the University Hospital, 51 patients, 27 per cent, were not treated. Many of these patients had no clinical evidence of metastases or inoperability that could be determined from examination of their records. Fifty-eight patients, 31.3 per cent, had only gastrostomies, with the appalling operative mortality of 45 per cent. The average length of life following gastrostomy was 4 months.

Forty-two patients, 22 per cent, had gastrostomy plus retrograde radium implantation. There was a 31 per cent mortality directly resulting from this procedure. Many of the deaths were due to traumatic perforation of the carcinomatous esophageal wall and subsequent mediastinitis and empyema. Other deaths were due to irradiation necrosis and subsequent mediastinitis. Still others died from the complications associated with the gastrostomy. Some of these patients also had supplementary irradiation therapy. This procedure was the procedure of choice from 1935 to 1938 and included the most favorable group of patients with regard to the likelihood of

response to treatment. The length of life following treatment in this group was 4.8 months. Eighty per cent of these patients had no clinical evidence of metastases as determined by clinical examination, including exploration of the upper abdomen at the time of the gastrostomy. No cures were obtained in this group. Ten patients, 5.4 per cent, had irradiation therapy alone. Among this group, 1 patient is alive  $3\frac{1}{2}$  years following treatment. This was a patient having a lye stricture in which there is some doubt as to whether he actually had a carcinoma. During this 10 year period there have been 6 esophagectomies, with a mortality of 50 per cent, and 5 other thoracotomies in which the lesion was found to be inoperable. This mortality is lower than the mortality percentage reported by Ochsner and DeBakey in a series of 58 esophagectomies from the literature, which was 70.6 per cent. Within the past 6 months there have been 4 successful transpleural esophageal and gastric resections with esophagogastric anastomoses, and there has been no mortality. A fifth patient was found to be inoperable by this approach.

The technique of the transpleural partial gastric resection and resection of the distal end of the esophagus with esophagogastric anastomosis for carcinoma of the cardiac end of the stomach fulfills all the principles for a sound surgical operation, provided that enough of the stomach can be brought up into the chest to permit an anastomosis without tension following a sufficiently wide resection of the carcinoma. There is an excellent exposure. The regional lymph nodes can be included in the resection. Furthermore, the esophagogastric continuity is restored, so that the patient may eat normally and not be subjected to the disadvantages and the inconveniences of a gastrostomy for the remaining period of his life.

The Torek operation for carcinoma located elsewhere in the esophagus also allows wide resection of the carcinoma and of the regional lymph nodes, but it provides no means for reestablishment of the esophagogastric continuity. The cervical esophagostomy can be connected to the abdominal gastrostomy in 2 ways. The first is by a rubber tube. These rub-

ber tubes are an unending source of complaints. They frequently become dislodged from the esophagostomy or the gastrostomy opening and become plugged with debris. The second way of re-establishing a passageway between the esophagostomy and the gastrostomy is by means of an anterior thoracic esophagoplasty utilizing skin tubes which are anastomosed to the esophageal stoma above and either to the stomach, a gastric tube (Beck-Jianu) or a segment of jejunum below which in turn may be anastomosed to the stomach.

These operations are difficult to perform, necessitate multiple operations with a high mortality and function well afterward in only a small number of cases. In a collected series of cases of anterior dermatoesophagoplasties reported by Ochsner and Owens an average of 4.5 operations per case with an operative mortality of 30 per cent was found. Of the entire group 56.6 per cent of the esophagoplasties were never completed. The authors warned of the danger of digestion of the skin tube by gastric contents with consequent gangrene and fistula. In a series of 36 cases in which the jejunum was utilized in forming an anterior cutaneous jejuno-esophagoplasty there was a 46 per cent mortality; only 43.3 per cent of the cases were completed. The greatest complication in this group was interference with the circulation of the mobilized segment of jejunum, resulting in gangrene. In 70 cases in which jejuno-dermatoesophagoplasty was carried out there was an average of 4.3 operations per patient and a 22.7 per cent mortality. In 55 per cent of the patients, the operation was not completed.

Consequently up to the present time, even though a patient may be freed of carcinoma of the esophagus by an esophagectomy the likelihood of again swallowing satisfactorily is quite remote. Any procedure that could be devised to combine complete removal of the carcinoma of the esophagus with the regional lymph nodes, and allow re-establishment of the esophagogastric continuity that did not necessitate a large number of operations for its completion and did not have a prohibitive mortality would certainly be a step forward in the surgical management of this disease.

With this goal in mind, 3 series of animal experiments (in dogs) were carried out in an attempt to fulfill these requirements. This article is a preliminary report of these experiments.

### EXPERIMENTAL DATA<sup>1</sup>

#### I. RECONSTRUCTIVE INTRA-THORACIC ESOPHAGOGASTRIC ANASTOMOSES

In the first series of experiments the esophagogastric continuity was restored by the construction of a greater curvature gastric tube which was anastomosed to the proximal esophagus at a subsequent operation. The operation was divided into two stages. The first stage performed through an abdominal incision, under drop ether anesthesia, consisted of isolating a gastric tube from the greater curvature of the stomach similar to that described originally by Jianu and lately by Carter and associates. The tube extends from about 5 centimeters proximal to the pylorus to within 4 centimeters from the cardiac orifice of the stomach. The tube was originally made by making a small opening through both the anterior and posterior walls of the stomach approximately 2.5 centimeters from the greater curvature. Two rows of curved hemostats were then applied, including both the anterior and posterior walls of the stomach within the jaws of the hemostats, and the stomach was then cut between the hemostats. The hemostats were then removed one by one from above downward, while a hemostatic layer of continuous No. 0 duxol suture was inserted. This was followed by a continuous inverted layer of sutures. An occasional interrupted silk suture was then used wherever reinforcement of the suture line was needed. By this technique gastric tubes measuring 20 to 30 centimeters in length have been made. Both ends were left attached to the stomach so that the lumen of the tube communicated with that of the stomach. The spleen was removed in order to allow greater mobilization of the gastric tube at the second stage of the operation.

At the second stage, usually 2 weeks after the first a thoracotomy was done under pos-

<sup>1</sup>Dr. Alfredo Casapelli, Rosario, Argentina, Dr. Juan S. Viera, Montevideo, Paraguay and Mr. James Tracy, Ann Arbor, Michigan, were most helpful in the performance of the experiments.

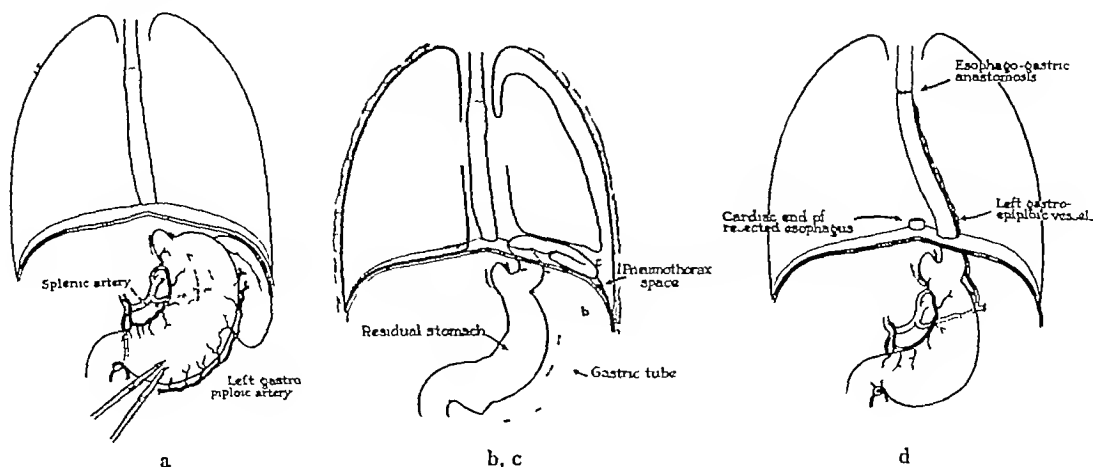


Fig 1 a, Line drawing illustrating the construction of a long gastric tube from the greater curvature of the stomach b and c, Line drawing illustrating the placing of the greater curvature gastric tube through a new diaphragmatic hiatus

tive pressure intratracheal ether anesthesia, the seventh rib on the left side being removed. The esophagus was partially resected, the lower end being inverted. An incision through the diaphragm was then made, beginning approximately 2 centimeters lateral to the esophageal hiatus and extending laterally along the course of the muscle fibers. The gastric tube was then transected at the pyloric end, the stomach closed, and the tube with its mesentery and the included gastroepiploic vessels brought up into the chest. The diaphragm was closed with interrupted sutures up to the new hiatus. At this location the diaphragm was sutured to the gastric tube in order to prevent subsequent herniation of the abdominal contents into the chest and in order to take tension off the tube. An end-to-end anastomosis was then made between the end of the esophagus and the gastric tube (Fig 1d). The mediastinal pleura was sutured to the gastric tube over the anastomosis in order to re-enforce the suture line and to relieve tension. In many of the operations the gastric tube was sutured to the prevertebral fascia to relieve tension. This, however, was not always necessary, since the gastric tube was frequently redundant enough to relieve all tension. Five grams of sulfanilamide was placed about the anastomosis. The lungs were gently and slowly inflated by means of positive pressure anesthesia and the

into a left pneumothorax space. d, Line drawing illustrating the formation of the esophagogastric anastomosis between the proximal end of the esophagus and the gastric tube.

chest wall was closed. A urethral catheter connected to wall suction was left in the chest during closure in order to insure the complete evacuation of all the residual pneumothorax air.

During the second stage of this operation, certain disadvantages and technical difficulties were encountered. The first disadvantage was that during the 2 week interval between the first and second stages, frequently so many adhesions developed between the tube and the remaining stomach and adjacent structures that the freeing of the tube was technically very difficult and time consuming. The second disadvantage was that in order to have an adequate exposure for the abdominal part of the operation through a thoracic incision, a rib had to be removed (usually the seventh or eighth) which was much too low to give adequate exposure for making a high esophagogastric anastomosis, at which time it would be of advantage to have the fourth or fifth rib resected.

Consequently, the operation was modified so that, at the first stage, the greater curvature gastric tube was divided at the pyloric end (Fig 1a). This end was carefully closed and the tube was examined to make sure that an adequate blood supply was present. A small opening was then made in the diaphragm, approximately 2 centimeters lateral to the esoph-

ageal hiatus, a left pneumothorax was obtained, and the gastric tube was placed in the left hemithorax as demonstrated in Figure 1b and c. Four interrupted sutures were then placed between the tube and diaphragm to hold the tube in place and to prevent other viscera from herniating into the chest. Care must be exercised not to close the hiatus too tightly, thereby impairing the circulation of the gastric tube.

With this modification, any desired rib may be resected at the second stage, since the abdomen is not reopened. The operating time was reduced as much as an hour or an hour and a half. Following resection of the esophagus the gastric tube is readily available for anastomosis. Furthermore, with the fourth or fifth rib resected the anastomoses could be made at a much higher level than originally, as is noted in the roentgenogram in Figure 1b in which the anastomosis was just 2.5 centimeters below the apex of the left hemithorax. (Also see the gross specimen in Figure 2a in which the anastomosis is at the level of the arch of the aorta.) If following resection of the esophagus at the second stage the gastric tube is not long enough to be anastomosed to the esophagus without undue tension the tube can be freed at the previously made diaphragmatic hiatus and additional tube or even stomach, can be brought up into the chest.

Furthermore the technique of performing the anastomosis was changed from the use of an inner continuous layer of catgut and an outer layer of interrupted silk to two layers of interrupted silk. This was felt to give better apposition of the ends, less interference with the blood supply and a more satisfactory anastomosis. Lately because of the fact that the gastric tube has occasionally had a brawny ridge at its end where the tube had been sutured at the first stage and because this ridge made inversion difficult during the performance of the end-to-end anastomosis, the anastomosis has been made between the end of the esophagus and the anterior aspect of the gastric tube approximately 2 centimeters from its end.

**Complications.** The number of difficulties experienced in experiments such as these upon

dogs is tremendous. The important advantages of the facilities of a hospital and reoperation of the patient in the postoperative treatment were necessarily absent in the experimental work. Many of the difficulties encountered during the early part of the experiments were recognized and corrected. The operation is technically difficult. The operative time was originally long and the blood loss considerable. Several of the first dogs died of operative shock.

The mediastinum in dogs is very labile, consisting of only the two layers of mediastinal pleura in many places. Great care must be exercised to prevent a bilateral pneumothorax, which dogs tolerate extremely poorly. Postoperative pulmonary complications occur at considerable frequency and their treatment necessitates constant and conscientious care to prevent postoperative atelectasis, pneumonia, pleural effusion, pneumothorax, and emphysema. Postoperative pulmonary complications (pleural effusion, atelectasis, and pneumonia) were the cause of death in 5 of the dogs during the early stages of the experimentation, before a very stringent postoperative regimen was instituted.

Because of the anatomical arrangement of the gastroepiploic vessels in dogs the amount of supporting tissue with the included vascular supply to the tube is considerably more bulky in dogs than in human beings. In the dog there are 3 or 4 left gastroepiploic vessels arranged in a fan-shaped manner in relation to the greater curvature in contrast to the human arrangement of one well defined left gastroepiploic vessel arising from the splenic and running parallel to the greater curvature. Consequently the gastric tube cannot be placed as high in the mediastinum in dogs as it can be in men because the pyloric end of the gastric tube can reach only as far as the level of the blood vessel to the pyloric end of the stomach permits. Furthermore in bringing the gastric tube into the chest, it is necessary to transport a considerable amount of supporting omental tissue with the included vessels. This mass of tissue is an annoying source of exudate. Also if this is too bulky it frequently prevents complete re-expansion of the lung. In the one esophagogastric anastomosis

done in a man, the tube was the same width as the normal esophagus and was placed upon the esophageal aspect of the aorta. There was no protrusion of the tube into the hemithorax whatsoever. This operation was done entirely in one stage. This was at a time when the technical difficulties involved in leaving the gastric tube within the abdomen at the first stage of operation were realized, but before any experience had been obtained with placing the gastric tube within the chest at the first stage, as was done subsequently in the modification of the experimental technique. The esophagogastric anastomosis in this patient was made at the level of the aortic arch. Death occurred on the 12th day after operation as a result of a perforation of the anastomosis with subsequent mediastinitis and an encapsulated mediastinal empyema which had been inadequately drained.

The greatest difficulty encountered in dogs is the gastric acidity, which is about twice as high as that in a normal man. Because of this factor they tend to digest catgut sutures, unless given something to buffer the gastric acidity. This high acidity was felt to be the responsible factor in the cause of death in the only 3 dogs in which disruption of the anastomoses occurred. These dogs died on their 3d and 4th postoperative days. Necropsy examinations revealed practically no catgut sutures about the anastomoses. Furthermore, there was digestion of the terminal esophageal mucous membrane. This occurred during the period of experimentation when the dogs were not given anything to eat or drink after operation, but were maintained entirely on intravenous fluids for the first 3 or 4 days.

**Postoperative treatment Shock** As a result of the modification of the operative technique by which the gastric tube was placed within the chest at the first operation, the operative time was markedly reduced, and the blood loss decreased. Shock was not a troublesome factor from then on. Immediately following the operation and twice daily thereafter for 3 or 4 days, 200 cubic centimeters of 5 per cent glucose and 200 cubic centimeters of Ringer's solutions were given intravenously.

**Pulmonary** Because of the tendency to pulmonary complications, a very stringent

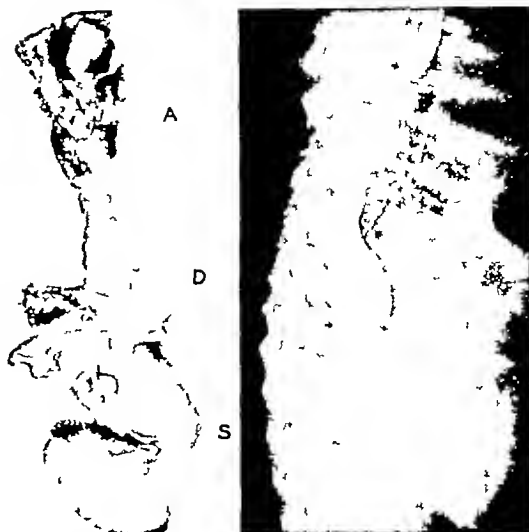


Fig 2 a, left, Dog 12 Gross specimen of an esophagogastric anastomosis made at the level of the aortic arch A, Anastomosis, D, diaphragm, S, residual stomach b, Dog 13, postoperative roentgenogram of an esophagogastric anastomosis made  $1\frac{1}{2}$  inches below (upper arrow) the apex of the left hemithorax Lower arrow indicates the new diaphragmatic hiatus This had been made too small with resulting partial obstruction

regimen was instituted. This consisted of giving carbon dioxide inhalations every 2 hours until 11 o'clock at night for the first 2 or 3 postoperative days, in order to assure complete re-expansion of the lungs and to prevent postoperative atelectasis and pneumonia. Frequent examinations of the chest were necessary to detect the presence of fluid. If present, thoracentesis was done twice daily until fluid no longer formed. Each dog was given 2 or 3 grams of sulfanilamide daily for the first 3 or 4 days.

**Gastric acidity** After the need to buffer the high gastric acidity that was present when the dogs were not fed was recognized, frequent small feedings were given every 4 hours for the first 6 postoperative days, these feedings consisted of 50 to 100 cubic centimeters of milk, 30 cubic centimeters of amphotel and  $1/400$  grain of atropine. After this regimen was instituted, there were no deaths as a result of disruption of the anastomosis.

Whereas the digestive factor in dogs is troublesome, this difficulty is not expected in human patients. Five of the last 6 patients with carcinoma of the esophagus seen at this





Fig. 3. a, Dog. Postoperative roentgenogram, 4 days, showing obstruction at diaphragm. Obstruction due to impacted air dust in stomach. b, Gross specimen showing well healed esophagogastric anastomosis. E, Esophagus. EG, anastomosis. GT, gastric tube. c, Macroscopical section of the esophagogastric anastomosis shown in Figure 2b, 5 days.

hospital during the past several months had no free hydrochloric acid in either the fasting specimen or after histamine injection; the sixth had no free hydrochloric acid in the fasting specimen but did have following histamine injection. Though hydrochloric acid is not the only factor involved in digestion, it is an important index of the state of function of the gastric mucosa in such patients.

**Results.** A series of 2 dogs have had the complete operation. There were no deaths following the first stage of the operation except perhaps one which might possibly be so considered. This dog (No. 13) died just before the beginning of the second stage of the operation after he had been placed upon the operating table. This was 2 weeks after the first operation. The cause of death could not be definitely determined. However several points of value were derived from this case.

The gastric tube in this dog had been made very long so as to demonstrate the possibility of making an anastomosis to the venous end of the chest. Even though the dog had died, the anastomosis was performed and the postoperative roentgenogram shown in Figure 2b was taken. The main point of interest derived from this dog was the fact that the end of the gastric tube had reopened. In spite of this there was no evidence of pleural fluid or infection. It was felt that satisfactory healing had not taken place because the diaphragmatic hiatus had been closed too tightly and thereby caused partial impalement to the blood supply to the tube with poor healing. The tightness of the diaphragmatic hiatus is demonstrated at the lower arrow in Figure 2b which shows obstruction to the passage of barium at the level of the diaphragm. Because of scar tissue contraction, the lumen of the hiatus will become smaller than that originally made. As a result of this observation, the second stage of the operation in which jejunal tubes were used (as described in part III) was performed after a shorter interval between the first and second stages, usually a period of 7 to 10 days. This was before scar tissue contraction had taken place. If the hiatus at the second stage was then found to be too tight, it was made larger.

All the remaining deaths occurred after the second stage. In only the last 4 of the 12 dogs was the operation performed in its final form that is, the tube was placed within the chest at the first stage and the present postoperative regimen followed. Three of the dogs lived sufficiently long to allow complete healing of the anastomosis. The fourth died on the fifth postoperative day from a perforated peptic ulcer which, as far as could be determined, had nothing to do with the operative procedure. The anastomosis in this dog, seen in Figure 2a, showed excellent healing and was functioning perfectly up to the time of death. One dog died on its tenth postoperative day after having done very well of a diaphragmatic hernia and pulmonary atelectasis. Another died on the fifteenth postoperative day from an overdose of morphine given at the beginning of an operation designed to relieve a supposed obstruction of the tube at the di-

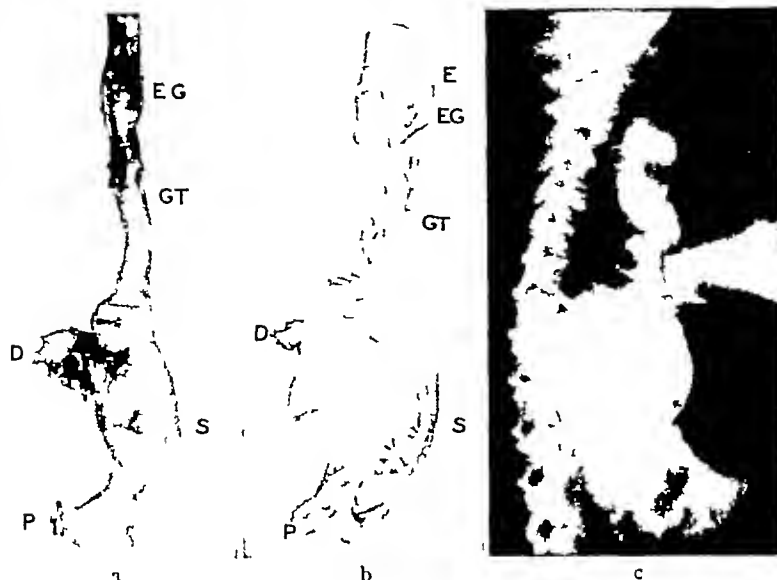


Fig 4 Dog 11 sacrificed 14 weeks after operation a Photograph of gross specimen of esophagogastric anastomosis and gastric tube before opening LG Anastomosis, GT, gastric tube, D diaphragm, S residual stomach, P pylorus b Same specimen photographed from within E Esophagus c Postoperative roentgenogram demonstrating widely patent anastomosis (upper arrow) and the propulsion of barium through the gastric tube into the stomach Lower arrow indicates junction of gastric tube and residual stomach

phragm as noted in the roentgenogram in Figure 3a. This dog had been eating both solid and soft foods very well until 2 or 3 days preceding death. Necropsy revealed that sawdust, which the dog had eaten from the floor of the cage, was impacted in the stomach and produced obstruction. The anastomosis was healed perfectly, as seen in Figure 3b and c. The fourth dog was sacrificed 14 weeks after operation. The dog had eaten very well, without vomiting. Postoperative fluoroscopic and roentgen examinations, Figure 4c, showed that barium by mouth passed readily from the esophagus through the tube into the stomach. Figures 4a and b are photographs of the gross specimen, which were made after this dog was sacrificed.

The results to date are certainly not conclusive but are suggestive of progress in the right direction. Many of the obstacles experienced at first have been overcome by subsequent modifications of the operative technique and particularly of the postoperative treatment. It has been gratifying to find that in only 3 of 12 cases has death been the result

of disruption of the anastomosis. These disruptions occurred, not because of some technical error in performing the anastomoses, but as a result of the high gastric acidity and digestive action found in dogs. These deaths occurred during a time in the experimentation when the dogs were receiving nothing by mouth after operation to buffer the gastric acidity.

*Physiological action of the gastric tube* The question arises, will these gastric tubes, which have been anastomosed to the esophagus in an antiperistaltic manner, function well enough to allow the patient to eat and maintain his weight? This can be answered only after more operations have been done, and the dogs observed over a long period of time. Dogs Nos. 9, 10 and 11, which lived for 10 days or more, were able to eat solid foods (canned dog foods) without vomiting if given in amounts not exceeding a tablespoon at a time. If the dogs were allowed to eat a larger quantity than this at one time they gulped the food and vomiting was common. The physiological action of the gastric tubes was studied by fluoroscopy and

roentgenograms after barium was given by mouth. The barium would immediately shoot into the stomach as a result of the propulsive force of the pharynx. No evidence of peristaltic action was noted in any tube in either the isoperistaltic or antiperistaltic direction. No difficulty is anticipated in the transportation of food from the esophagus into the stomach by means of the gastric tube because the pharynx has a strong propulsive action which tends to shoot the food through the tube and the force of gravity tends to make the bolus drop to the stomach. Also the fluctuating intrathoracic pressure tends to work with gravity in pumping the food into the stomach in case a large bolus is present. These views have been substantiated by studying this mechanism postoperatively by means of the fluoroscope. If strictures should develop at the anastomosis site they could be dilated.

**Clinical application.** As to the clinical application of reconstructing an esophagus by a tube made from the greater curvature of the stomach, it is obvious that the stomach must be large enough for the construction of such a tube. Frequently in patients with carcinoma of the esophagus, the stomach is small because of the inadequate filling of the stomach resulting from chronic obstruction of the esophagus. It is important that the size of the stomach be determined preoperatively by means of barium roentgenograms. If the stomach is small and the patient can drink fluids, it can frequently be redilated by forcing fluids up to 4000 to 5000 cubic centimeters per day for 4 to 5 days preceding operation. By so doing it has been possible in 3 patients to construct tubes 25 to 30 centimeters in length. If there is total esophageal obstruction however or if it is found impossible to redilate the stomach, then the operation is necessarily contraindicated.

If a suitable tube is to be constructed and mobilized in human beings it is important at the time of the first operation to have adequate exposure at three points. These three points are at the pyloric end of the stomach at the cardiac end of the stomach and also in the left upper quadrant in order to allow splenectomy. The most satisfactory incision has been a midline incision extending from the ensiform

cartilage to the umbilicus, and then laterally to the left costal margin. It is important that a splenectomy be done because the spleen and the splenic vessels, are somewhat fixed to the posterior wall. If the spleen is not removed adequate mobilization of the left gastrosplenic vessels, and in turn of the gastric tube is not possible. If only a short gastric tube is needed a splenectomy is not necessary. A jejunostomy at the first stage for feeding purposes should be considered.

If at the second stage the carcinoma is found to be inoperable the gastric tube can either be (1) left alone (2) brought out through the anterior angle of the incision as a gastrostomy or (3) if the case warrants, a palliative anastomosis can be made by transecting the esophagus above the level of the neoplasm, inverting the distal end and anastomosing the proximal end to the gastric tube so that the patient can continue to eat and live a more comfortable existence during his remaining life. There is just as much justification for restoring the esophagogastric continuity in a patient suffering with carcinoma of the esophagus as there is in performing an ileocolostomy in a patient afflicted with carcinoma of the bowel.

#### SUMMARY

1. **Indications** for the construction of an intrathoracic esophagogastric anastomoses are (a) a patient in good condition as to the state of nutrition, age and operative risk (b) a patient who barring complications, could have a relatively long life expectancy if the lesion is operable (c) a patient who has only partial esophageal obstruction and whose stomach is large enough to construct such a gastric tube. This would allow the patient to eat after the first stage of the operation, and to maintain his nutrition before the second stage.

The **advantages** of the operation are (a) probably the best method of re-establishment of the esophagogastric continuity and permitting all types of foods to be eaten (b) accomplished in two operations whereas the construction of an antethoracic cutaneous esophagostomy requires multiple operations (c) is not disfiguring to the anterior chest (d)

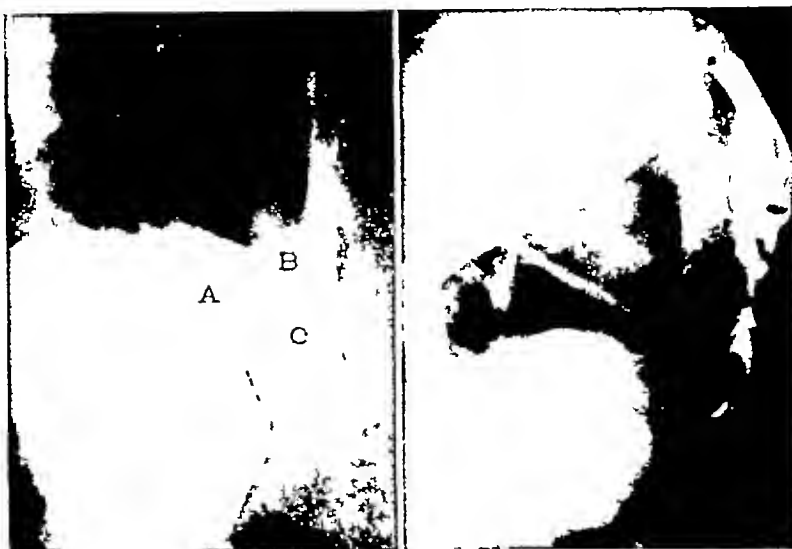


Fig 5 a, left, Postoperative roentgenogram of a patient in which a greater curvature gastric tube was placed beneath the anterior thoracic skin almost to the level of the angle of Louis. A, Base of gastric tube at junction with cardia of stomach (shown in fluoroscopy but not in this particular projection), B C, Position of three costal cartilages which might have been resected to decrease the distance from cardia of stomach to base of neck. b, Postoperative roentgenogram of an experimental antehoracic subcutaneous esophagoplasty carried out in one stage. Arrow points to site of anastomosis at level of manubrium.

following removal of the cancer, the gastric tube is immediately available for anastomosis, (e) an incision in the neck is not needed, (f) if the carcinoma is found to be irremovable, the gastric tube would permit a palliative sidetracking operation, (g) if, at the second stage of the operation, the gastric tube is found to be too short, the diaphragm can be reopened and additional tube and even cardia of stomach can be transported into the chest.

2 The *contraindications* are (a) debilitated patients, (b) poor operative risks, (c) long continued or total esophageal obstruction in patients in whom the stomach would be too small to allow construction of a suitable gastric tube.

The *disadvantages* are that (a) a major operation is required before the surgeon knows whether the cancer can be removed, (b) the operation would probably be associated with a higher operative mortality than a Forek operation because of the risk associated with the intrathoracic anastomosis.

The performance of an intrathoracic esophagogastric anastomosis between the upper

esophagus and a gastric tube made from the greater curvature of the stomach after resection of the esophagus for carcinoma appears to have certain merits if done in a selected group of patients. This group includes those patients who have only partial esophageal obstruction who are still able to swallow enough food to prevent atrophy of the stomach so that a gastric tube of sufficient length may be constructed. This also allows the patient to eat between the first and second stages of the operation. Furthermore, the patient should present a good operative risk.

The final decision as to the type of operation to be performed depends on whether the surgeon is willing to accept the added risk of an intrathoracic anastomosis in order to secure for the patient a normal means of passing food into the stomach rather than performing a Forek operation which requires gastrostomy feedings. The operative mortality of an esophagogastric anastomosis, using a gastric tube, would be no higher than a transthoracic esophagogastric anastomosis after resection of carcinoma at the cardiac end of the stomach. The

operative mortality would probably be higher than for a Torek operation but much less than the combined operative mortality of a Torek operation and a later antethoracic cutaneous esophagoplasty. Experience alone can determine the feasibility of the operative procedures that have been illustrated by the experiments reported in this article.

## II RECONSTRUCTIVE ANTETHORACIC ESOPHAGOGASTRIC ANASTOMOSIS

Many surgeons are of the opinion that the added risk of an intrathoracic esophagogastric anastomosis is not justified and that an anterior esophagoplasty should be done. As a result of studying the postoperative roentgenogram (Fig 5a) of a patient with a carcinoma of the esophagus in which a greater curvature gastric tube was constructed and brought out subcutaneously beneath the skin of the anterior chest wall certain modifications of the operative technique were suggested which might be employed to increase the length of the tube and consequently permit an anterior thoracic esophagoplasty to be done in one stage. The first modification was that the distance between the base of the tube at the cardia of the stomach and the anterior chest wall might be shortened if the cardia of the stomach was placed directly beneath the costal cartilages. This can be done by incising the peritoneum and diaphragmatic peritoneal fascia about the esophageal hiatus in order to allow the lower thoracic esophagus to be pulled into the abdomen. This in turn will allow the cardiac aspect of the stomach and the base of the tube to lie just beneath the costal cartilages. The second modification was that a considerable length of tube was wasted by having to descend and then turn around the costal margin B-C, before being tunneled beneath the anterior thoracic skin to ascend toward the neck. This angle may be greatly decreased by resecting the lower three costal cartilages just lateral to the sternum. If it is necessary to remove the spleen in order to allow sufficient mobilization of the left gastrophrenic vessels.

With these modifications in mind animal experimentation was done to determine the feasibility of such a procedure and to see

whether it was anatomically possible. Only one dog was operated upon by the antethoracic esophagogastric anastomosis method but the procedure appears to have certain merit. Additional dogs were not operated upon because it is impossible to maintain a dog's nutrition by such a procedure. The increased distance to which this tube can be extended is illustrated by the postoperative roentgenogram (Fig 5b) which illustrates the antethoracic esophagogastric anastomosis in a dog made at the level of the manubrium. In this particular dog the cervical esophagus was transected at the level of the superior mediastinum. The distal esophagus was closed and dropped back into the posterior mediastinum. Following this an end-to-end anastomosis was made between the upper end of the esophagus and the antethoracic gastric tube and the cervical fascia and skin were then closed over it.

When the lower three costal cartilages are resected and when the diaphragm is pushed up or separated it is important that the left hemithorax should not be entered. Opening of the pleura is less likely to occur in man because the mediastinum is wider than in dogs. If the pleural cavity is accidentally entered the diaphragm should be sutured to the sides of the gastric tube to prevent herniation of the abdominal viscera into the thorax during the postoperative period.

There are at least three situations in which an antethoracic esophagogastric anastomosis appears feasible. (1) In patients having a highly situated neoplasm when there may be some doubt as to whether the upper esophagus could be reached for anastomosis with an intrathoracic gastric tube. If after construction of the tube the tube is too short for an antethoracic anastomosis the remaining gap would have to be bridged by a skin tube. (2) Patients for whom the added risks of an intrathoracic anastomosis would be unwise. (3) As a palliative measure in patients who have been found to have metastases or who are believed to be inoperable.

If possible the antethoracic cervical esophagogastric anastomosis should be done at the same operation at which the gastric tube is formed rather than creating a high thoracic

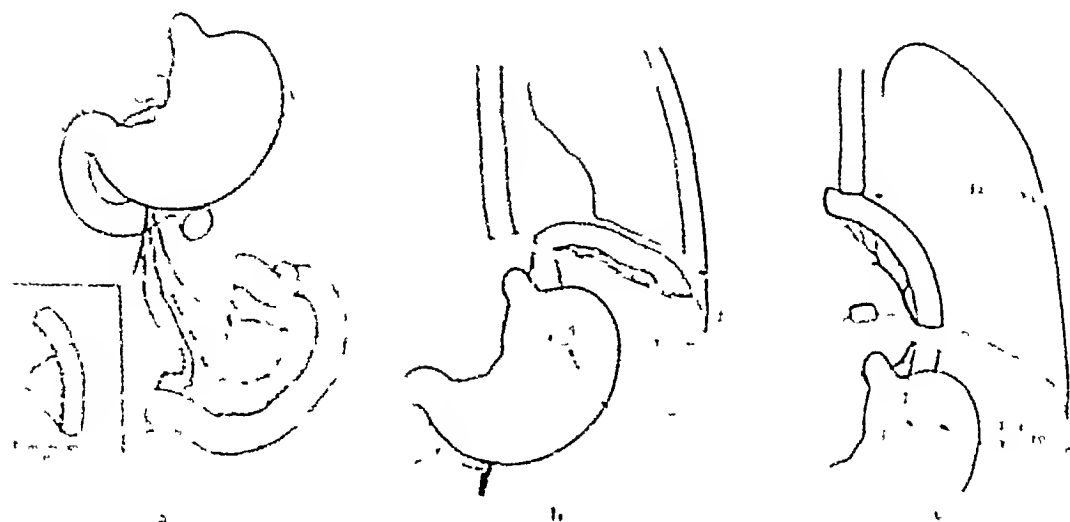


FIGURE 6. a. Drawing illustrating the formation of a jejunocolic fistula. b. Drawing illustrating the formation of a jejunocolic fistula. c. Drawing illustrating the formation of a jejunocolic fistula.

of the jejunal limb. d. The jejunal segment within a left pleural space. e. Line drawing illustrating the formation of a jejunocolic fistula.

gastrostomy at a first operative stage and the anastomosis at a second stage. The reason for this is the fact that when the gastrostomy end remains upon the skin surface for a period of several days it becomes edematous, brown, and secondarily infected and would then be relatively unsuitable for use in the formation of an anastomosis.

It is best to do a primary anastomosis between the gastric tube and the upper esophagus; the tissues of which are known to be compatible rather than by using an intervening skin tube which tolerates gastric juice poorly. It is felt that an intrathoracic anastomosis would function better than an antethoracic anastomosis.

Since performing these experiments, it has been noted that Halpern in 1912 was successful in performing an antethoracic esophago-plasty in dogs by utilizing a greater curvature gastric tube.

### III. RECONSTRUCTIVE INTRATHORACIC ESOPHAGOGASTRIC ANASTOMOSIS

As was stated previously, in many patients having had long continued obstruction of the esophagus, the stomach is so small as to preclude the construction of a greater curvature gastric tube of adequate length and caliber

In such cases esophagogastric continuity may be re-established after resection of the diseased portion of the esophagus by the utilization of a segment of jejunum, as illustrated in the diagrammatic representations in Figure 6.

The jejunum has been employed previously by a number of investigators in antethoracic subcutaneous esophago-plasty usually in conjunction with a skin tube (7). In the series of experiments to be described, a segment of jejunum was utilized for an intrathoracic anastomosis between the esophagus and the stomach. The operation was divided into two stages.

The first stage consisted of isolating a segment of jejunum approximately 18 to 24 centimeters in length. This segment was isolated in most of the experiments 3 to 4 feet below the ligament of Treitz. This distance was used because of the anatomical arrangement of the blood vessels in this area. The primary arches of the intestinal blood vessels are considerably larger here than elsewhere and the distance between the primary and secondary arches is greater and the arches run for a greater distance parallel to the intestine proper in this location than in the more proximal jejunum. Another reason for selecting a segment of jejunum 3 to 4 feet from the ligament of



Fig. 7. a, left, Dog 3. Postoperative roentgenogram demonstrating good function of the esophagojejunostomy and gastrojejunostomy. (The esophagojejunostomy as made at the level of the upper arrow but after operation descended in the chest to the level of the middle arrow.) Lower arrow indicates position of the posterior gastrojejunostomy. b. Gross specimen, jejunum, demonstrating the jejunal tube anastomosed between the esophagus and the stomach as shown in the roentgenogram in a. ES, End-to-side esophagojejunostomy; J, jejunal tube; GJ, gastrojejunostomy; S, residual stomach; P, Pylorus.

Treitz is that the mesentery is longer in this region than it is higher and it allows greater mobilization of the jejunal segment. Occasionally a primary arch is sectioned proximal to its anastomosis with the adjacent arch in order to obtain a greater length of jejunal segment. A site is chosen in respect to the blood supply which will allow a long proximal limb to be placed in the chest in comparison with a shorter distal limb that is to be anastomosed to the stomach. The mesentery is divided next to the vessels, as diagrammatically shown in Figure 6a, care being taken not to injure the vascular supply to that particular segment. The jejunum is then reunited by an end-to-end aseptic anastomosis.

The isolated jejunal segment with its blood supply is placed through a small opening in the transverse mesocolon into the lesser omental bursa. The distal end is anastomosed (Figure 6b) to the posterior aspect of the stomach approximately 3 to 4 centimeters below the esophageal hiatus either by an end-to-side or side-to-side anastomosis. The latter is better

in dogs because of the small caliber of the jejunum. The longer proximal limb of the jejunal segment is then carefully inspected and if the circulation appears adequate, the end is carefully closed with two layers of interrupted silk. If there are any color changes the impaired area is resected to normal tissue and the new end is closed. A small incision is made in the left diaphragm 2 centimeters lateral to the esophageal hiatus, and the long proximal limb of the jejunal segment is inserted into the pneumothorax space that was obtained in the left hemithorax when the diaphragm was opened. The jejunal tube is fastened to the new hiatus in the diaphragm by three to four interrupted sutures.

The second stage is performed in from 1 to 2 weeks, at which time the esophagus is partially resected and the upper end of the esophagus anastomosed in an isoperistaltic manner to the end or the side of the jejunum—the end-to-side anastomosis gives a larger stoma (Fig. 6c). The remainder of the operation is similar to that in which the gastric tube is used. The same postoperative treatment as used in the experiments with gastric tubes is employed in this series.

The one disadvantage of this procedure in comparison with a gastric tube is that the intrathoracic anastomosis must necessarily be at a lower level than that obtained with a gastric tube because a jejunal tube cannot be made as long as a gastric tube without impairing its blood supply. The intrathoracic anastomosis with a jejunal tube can be made at least as high as, or slightly higher than, the level of the hilum of the lung whereas with the gastric tube method the entire thoracic esophagus can be resected. In one dog however the esophagojejunostomy was made at the level of the aortic arch, and further research may develop a technique by which a longer jejunal tube can be satisfactorily constructed.

Occasionally one is surprised at the second stage of the operation to find that a long tube has become considerably shortened as a result of disuse atrophy. The longest proximal limb of jejunal segment placed into the thorax in our experiments, so far, was 23 centimeters. From examinations of necropsy material it appears



Fig 8 a, left, Dog 5 Postoperative roentgenogram demonstrating the esophagojejunostomy just below the level of the aortic arch (upper arrow) Lower arrow indicates the position of the posterior gastrojejunostomy b, gross specimen, 6 weeks, demonstrating the long jejunal tube anastomosed between the esophagus and stomach E, Esophagus, EJ, end-to side esophagojejunostomy, JT, jejunal tube, D, diaphragm, GJ, gastrojejunostomy, S, residual stomach P, pylorus

that a comparable length of jejunum can safely be isolated in human patients

**Results** Only 5 dogs have been operated upon according to this technique. There was only 1 operative death. This was on the ninth postoperative day as a result of an empyema. The necropsy examination showed the anastomosis to be well healed. All the remaining dogs lived and ate satisfactorily. One was sacrificed postoperatively because of pain from abdominal distention which was thought to be due to intestinal obstruction, but at necropsy was found to be the result of a hugely dilated stomach. Both the gastrojejunal and the esophagojejunal anastomoses in this dog showed perfect union. The other dogs were sacrificed 6, 10, and 12 weeks, respectively, after operation. All the gross specimens from these dogs showed excellent healing of the anastomoses and widely patent stomas. Figures 7 and 8 demonstrate the postoperative roentgenograms and the gross specimens of dogs No 3 and No 5 of this series. Fluoroscopic examination of these dogs revealed peristaltic action in the jejunal tube.

The inferior results obtained in the series of dogs in which a gastric tube was used, as compared with the series in which a jejunal tube was used, are explained by the fact that the jejunal series was the last series of dogs to be operated upon. By this time more experience had been obtained in the postoperative management of these cases.

#### SUMMARY

A preliminary report, based upon animal experimentation, of operative techniques for the re-establishment of the esophagogastric continuity by intrathoracic and antethoracic anastomoses between the upper esophagus and gastric or jejunal tubes has been presented. This work is still in its initial stage and many more operations must be performed before conclusive results can be presented. If subsequent investigation proves that these techniques are of value, much progress will have been made in the surgical management of patients with carcinoma of the esophagus in restoring them to a state in which they can again enjoy the pleasures of eating. The ad-





# GRANULAR CELL MYOBLASTOMA

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IN 1926 Abrikossoff first called attention to a peculiar tumor which he termed myoblastic myoma and which he thought was derived from striated muscle. It was considered to be a rare tumor until in 1934 Klemperer reported 6 cases and collected 38 others from the literature. Since that time many additional reports have appeared under various names: myoblastoma (Klemperer), rhabdomyoma granulocellulare (Diss), rhabdomyoma and granular cell myoblastoma.

Gray and Gruentfeld again reviewed the literature in 1937, bringing the total of reported cases to 77, including 5 of their own. They tabulated the distribution of these neoplasms. The proximal part of the alimentary tract in general and the tongue in particular were the most common sites, although the tumors were widely distributed throughout the body. Table I reproduces Gray and Gruentfeld's list with the addition of a number of subsequently reported cases and 30 tumors studied in the Laboratory of Surgical Pathology of Columbia University since 1929. This table does not include all of the reported cases of granular cell myoblastomas of the tongue, which have been recorded by Thoma.

The 30 examples studied in this laboratory include tumors arising in a wide variety of sites. Since tumors of this type in the middle ear and external auditory canal have not been previously reported, the data available concerning 2 cases occurring in this region encountered at the Presbyterian Hospital will be recorded.

## CASE REPORTS

CASE 1. S.P. 43344, Unit Hist. 260291. R. M., a 60-year-old white female, was admitted to the Ear, Nose and Throat Service of the Presbyterian Hospital, New York, on June 26, 1930, complaining of intermittent bleeding from the ear over a period of more than 20 years. The lesion had been operated

upon at least four times previously, first in Rumania shortly after the complaint developed. Examination revealed a large, smooth, pedunculated tumor filling the external auditory canal. It was removed in two pieces with a snare by the late Dr. Cornelius G. Conkley. Twenty-five months later when the patient was last seen, there was no evidence of recurrence.

The specimen consisted of two resilient nodules of grayish white tissue showing areas of hemorrhage. They measured 1.5 by 1.0 by 1.0 centimeter and 1.3 by 0.5 by 0.5 centimeter respectively. Histologically the neoplasm was composed of closely packed large pale cells with granular acidophilic cytoplasm and regular relatively small centrally placed nuclei. A delicate stroma containing numerous capillaries, segregated the tumor cells into small rounded nests. Mitotic figures were not observed, nor were cross or longitudinal striations. With the Scharlach R stain no lipid was demonstrable (Fig. 1).

(Case 2. S.P. 8404, Unit Hist. 677455. I. R., a 77-year-old white female was admitted to the Ear, Nose and Throat Service of the Presbyterian Hospital, New York, on June 15, 1932, complaining of a discharge from the right ear of 8 years' duration. Six years before, she had suffered a spontaneous facial paralysis with nystagmus. For 2 weeks the ear had been painful and bleeding. Other symptoms were deafness, dizziness, and difficulty with swallowing on the right side. Examination revealed a purulent discharge and a polypoid mass filling the external auditory canal. X-ray films demonstrated clouding in the mastoid region. A radical mastoidectomy was performed. Bleeding was copious and, because of it, the operator could not be certain whether the tumor arose from the middle ear or the external auditory canal.

The tumor was bilobed, the larger lobe measuring 1.5 by 0.7 by 0.6 centimeter. Part of the tumor was histologically a characteristic granular cell myoblastoma (Fig. 2). Other portions showed marked edema and were extremely vascular, the tumor cells being few in number and widely separated (Fig. 3). In these areas the cells showed a striking perivascular arrangement.

These two tumors appear to be characteristic granular cell myoblastomas. Although patient in Case 1 has been lost to follow-up after only 25 months and patient in Case 2 has just been operated upon, the long dura-

From the Surgical Pathology Laboratory, College of Physicians and Surgeons, Columbia University, and the Department of Surgery, Presbyterian Hospital, New York.

\*This case is reported with the permission of Dr. John D. Kernan.

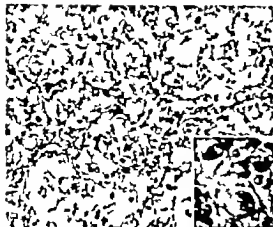


Fig. 1. Case 1. Granular cell myoblastoma of the external auditory canal. Hematoxylin and eosin stain.  $\times 70$ . The section in the inset shows the granular character of the tumor cell cytoplasm. Masson trichrome stain.  $\times 400$ .

tions prior to operation are illustrative of the essentially benign nature of this type of neoplasm. Nevertheless they may recur if incompletely excised, as indicated in the history of Case 1. This was observed in one other case in our series, that of Herman and Cracovener with involvement of the vocal cord, which recurred 2 months after the first removal. However the patient was followed for 2 years after the second operation with no further recurrence. There has been no evi-

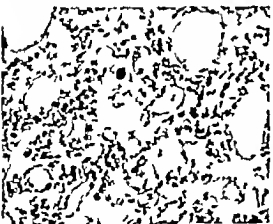


Fig. 2. Case 2. Granular cell myoblastoma of the external auditory canal. This portion of the tumor is highly vascular and contains few granular cells, which are widely separated and tend to be grouped about blood vessels. Hematoxylin and eosin stain.  $\times 70$ .



Fig. 3. Case 2. Granular cell myoblastoma of the external auditory canal. The tumor cells are arranged in a suggestive organoid pattern. Hematoxylin and eosin stain.  $\times 70$ . The inset shows the characteristic granular character of the tumor cell cytoplasm. Masson trichrome stain.  $\times 400$ .

dence of malignancy in any of our 20 cases, but follow up data are available in only 14. Of these 1 patient died with nephritis shortly after excision of a subcutaneous myoblastoma of the back. The 13 other patients have been well and without evidence of recurrence for periods varying from 4 months to 9 years, 3 for more than 5½ years and 5 for from 2 to 4 years. A number of malignant tumors have been reported under the name myoblastoma, but it seems doubtful whether they should not be classified more properly as rhabdomyosarcoma. Von Mevenburg's case of "myoblastic sarcoma" included in Klempner's series is an example. It is described as showing atypical cells and numerous mitotic figures, findings which are not observed in what is generally accepted as the characteristic granular cell myoblastoma.

Klempner called attention to the active proliferation of the squamous epithelium overlying these tumors when they occur in the skin or just beneath a mucosal surface. This was present in 7 of our cases, 3 of the tongue, 2 of the vocal cord, and 1 each of the trachea and skin of the gluteal region. Several cases have been reported as examples of coincidental myoblastoma and squamous cell epithelioma. Indeed in one of our cases the diagnosis of squamous cell epithelioma of the tongue was made in another hospital on biopsy and re-



Fig 4 Granular cell myoblastoma of the muscles of the thigh. The organoid arrangement of the granular cells in small nests, separated by a delicate, vascular stroma, simulates the appearance of endocrine gland neoplasms. Hematoxylin and eosin stain  $\times 135$ . In the inset cytoplasmic granules are few and small but distinct. Masson's trichrome stain  $\times 385$ .



Fig 5 Above Granular cell myoblastoma of floor of mouth. The granular cell contains longitudinal striations suggesting myofibrils. Masson's trichrome stain  $\times 620$ .

Fig 6 Below Granular cell myoblastoma of the floor of the mouth. The ribbon like cell shows parallel cross-striations at one end and, at the opposite end, numerous granules. Masson's trichrome stain  $\times 620$ .

dium treatment given before the patient came to this institution and the correct diagnosis of granular cell myoblastoma was established by excision. This case also provides evidence of the marked radioresistance of this type of neoplasm, since the tumor cells survived a sufficient dosage of radium to produce necrosis of the tongue.

In the tumors of this group there is great variation in the number, size, density, and depth of acidophilic staining of the characteristic granules. Paucity of granules in a given tumor may give rise to difficulties in diagnosis, especially when combined with an organoid pattern of growth which has been observed in a number of instances, including

TABLE I

	Tongue	Lip	Alveolar process of maxilla and mandible	Floor of mouth	Upper esophagus	Larynx and vocal cord	Trachea and bronchus	Skin	Subcutis	Muscles of extremities	Vulva	Breast	Orbit	External auditory canal	Total
Klemperer	21	1	6		1	4		7		2		2			44
Gray and Gruenfeld	13	1				4		2	3	6		4			33
Szathmáry											1				1
Freneckner	2	1				1	1								5
Von Bahr													1		1
Leroux and Delarue	2		1												3
Kramer							1								1
Tambs and Kowles											1				1
Grayzel and Friedman									1						1
Kratochvil			1												1
Authors'	5	1	2	1		1*	1	3	10	1		2		2	29*
	43	4	10	1	1	10	3	12	14	0	2	8	1	2	120

\*One of the lesions in the Presbyterian Hospital series, a granular cell myoblastoma of the vocal cord, has been previously reported by Kernan and Cracovaner and is included in Gray and Gruenfeld's summary.

Klemperer's 6th case and 4 of the case in our series. Growth of this type show a striking perivascular arrangement of the granular cell with relation to numerous, thin walled capillaries simulating neoplasms arising from endocrine glands. Case 2 illustrates this organoid pattern of growth to some extent. It is much more striking, however, in two granular cell myoblastomas from the subcutaneous tissues of the arm and popliteal space respectively, and in 1 from the muscles of the thigh (Fig. 4).

The histogenesis of the granular cell myoblastoma has not yet been definitely established although most of the writers on the subject accept the theory of origin from myoblasts. This is suggested principally by the acidophilic cytoplasmic granules and the occurrence of ribbon-like syncytial masses. In addition, Vrikosoff and several later writers have described cross or longitudinal striations within granular cells or transitions between granular cells and striated muscle fibers. On the other hand numerous observers have been unable to confirm these findings. Klemperer offers as explanation for this confusion the close proximity of granular cells and normal muscle fibers when these tumors infiltrate striated muscle as they so frequently do. However he also describes, in one of his cases, an arrangement of granules in parallel rows suggestive of striations. The general experience in this laboratory has been substantially in agreement with Klemperer. Only 12 of our 30 granular cell myoblastomas were distinctly encapsulated the rest being infiltrating tumors. However in the case of a typical myoblastoma occurring in the floor of the mouth of a 35 year old male we have observed longitudinal striations suggestive of myofibrils (Fig. 5) and in isolated granular cells distinct parallel cross-striations (Fig. 6). Inasmuch as there is no striated muscle in the sections, there can be no doubt that these are tumor cells and not skeletal muscle cells. Therefore this observation appears as concrete evidence in support of the theory of the myogenous origin of these neoplasms. One other tumor occurring in the subcutaneous tissues of the deltoid region, showed sug-

gestive longitudinal traction and in pictures of scattered cells, a cross alignment of the granules without however distinct cross striations. In accepting the theory of the myogenous origin of the granular cell myoblastoma, one may suppose that the tumor occurring in sites where striated muscle is not normally present arise from embryonal rests of aberrant myoblastic tissue. It does not seem necessary to believe as Gray and Gruenfeld suggest, that these tumors are of myogenous origin in one situation and arise from some other tissue in other sites since their appearance and behavior are identical in all locations except when they assume the organoid pattern here described.

#### SUMMARY

Two cases of granular cell myoblastoma of the external auditory canal are reported and 30 cases of this type of neoplasm occurring in various body sites are reviewed. The finding of longitudinal and cross striations in an otherwise typical tumor of the floor of the mouth gives support to the generally accepted theory of the myogenous origin of these neoplasms. It is pointed out that some of the granular cell myoblastomas are highly vascular and have an organoid arrangement which may give them a resemblance to neoplasms of endocrine gland origin.

#### REFERENCES

1. Anagnostou, A. J. *Virchows Arch.* 14, 20.
2. Baur, G. *on Acta epith. Kbh.* 95, 16, 109.
3. Dinn, A. *Bull Assoc. J. Cancer* 9, 7, 8, 89.
4. F. v. C. *P. Acta Otol. Rhenol.* 95, 26, 104.
5. G. S. H. and G. L. W. *Arch. Path. & Bact.* 11, 1, 100.
6. G. S. H. and G. L. W. *Arch. Path. & Bact.* 11, 1, 100.
7. Klemperer, P. *Am. J. Cancer* 19, 1, 100.
8. Klemperer, P. *Am. J. Cancer* 19, 1, 100.
9. Klemperer, P. *Ann. Otol. Rhinol.* 19, 1, 100.
10. Klemperer, P. *Arch. Path. & Bact.* 11, 1, 100.
11. Klemperer, P. *Am. J. Cancer* 19, 1, 100.
12. Klemperer, P. *Ann. Otol. Rhinol.* 19, 1, 100.
13. Klemperer, P. *Arch. Path. & Bact.* 11, 1, 100.
14. Klemperer, P. *Am. J. Cancer* 19, 1, 100.
15. Klemperer, P. *Ann. Otol. Rhinol.* 19, 1, 100.
16. Klemperer, P. *Arch. Path. & Bact.* 11, 1, 100.
17. Klemperer, P. *Am. J. Cancer* 19, 1, 100.
18. Klemperer, P. *Ann. Otol. Rhinol.* 19, 1, 100.
19. Klemperer, P. *Arch. Path. & Bact.* 11, 1, 100.
20. Klemperer, P. *Am. J. Cancer* 19, 1, 100.
21. Klemperer, P. *Ann. Otol. Rhinol.* 19, 1, 100.
22. Klemperer, P. *Arch. Path. & Bact.* 11, 1, 100.
23. Klemperer, P. *Am. J. Cancer* 19, 1, 100.
24. Klemperer, P. *Ann. Otol. Rhinol.* 19, 1, 100.
25. Klemperer, P. *Arch. Path. & Bact.* 11, 1, 100.
26. Klemperer, P. *Am. J. Cancer* 19, 1, 100.
27. Klemperer, P. *Ann. Otol. Rhinol.* 19, 1, 100.
28. Klemperer, P. *Arch. Path. & Bact.* 11, 1, 100.
29. Klemperer, P. *Am. J. Cancer* 19, 1, 100.
30. Klemperer, P. *Ann. Otol. Rhinol.* 19, 1, 100.

# HEMORRHAGIC INFARCT OF THE TESTICLE IN THE NEWBORN

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**H**EMORRHAGIC infarct of the testicle in the newborn has been recorded only once in the English literature (Campbell). In that case, the child was operated upon for tumor of the left testicle, at the age of 2 months. Dry hemorrhagic gangrene was found. Subsequently it was learned that at birth a diagnosis of bilateral hemorrhagic orchitis resulting from obstetrical trauma had been made.

We have had the unusual experience of seeing two cases of hemorrhagic infarct of the testicle within a 3 month period. Both cases were diagnosed during the first week of life, and the infants were operated upon on the fourteenth and tenth days of life, respectively.

**CASE 1** Hospital No. B-17930, baby deB was admitted to the hospital July 19, 1941. The mother was a trigravida secundipara. The first baby died at 6 months of age with diarrhea. The second pregnancy terminated in a self induced abortion. Kahn test of mother was negative. This was a normal pregnancy, full term, vertex presentation, delivered on July 19, 1941, without any difficulty and without instruments. The mother had a severe postpartum hemorrhage and went into collapse. A transfusion of 500 cubic centimeters of citrated blood was given. The mother recovered and convalescence thereafter was uneventful.

The infant was born with a mass in the left scrotal sac. Physical examination otherwise was normal. The temperature was normal, and the birth weight was 3,575 grams. The scrotum showed irregular areas of ecchymosis. The left side of the scrotum was markedly swollen, and contained a globular shaped mass measuring approximately  $3\frac{1}{2}$  by 2 centimeters in size. The mass was smooth and fibro-elastic in consistency in contradistinction to the hardness associated with testicular tumor. The lower pole of the mass was adherent to the scrotum and did not transilluminate.

Laboratory examinations revealed blood group, O, hemoglobin 17 grams, red blood cells, 5,800,000, white blood cells, 15,500, differential white blood cell count—polymorphonuclear leucocytes 27 per cent, lymphocytes 70 per cent, large monocytes 3 per cent, bleeding time,  $4\frac{1}{2}$  minutes, clotting time,  $6\frac{1}{2}$  minutes, urine examination, normal, Aschheim

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Zondek test, negative, x-ray film of scrotum, non-contributory, x-ray film of chest, normal.

The child remained on the pediatric service under the supervision of Dr. Grover C. Powers. The child was breast fed. He was given hykinone 3.2 milligrams daily for the first 5 days after birth. A urological consultation was requested on the third day, and he was observed daily by the members of the urological staff for the next 11 days, during which time he gained weight to 3,600 grams on the eighth day of life, and then lost weight to 3,530 grams on the tenth day of life. During this period the child remained afebrile, the ecchymosis of the scrotum disappeared, but the size of the mass in the scrotum and the consistency of the mass remained unchanged. A diagnosis of hemorrhage into the left tunica vaginalis was made. On the fourteenth day of life, an exploration of the left side of the scrotum was carried out.

At operation an incision was made over the left external inguinal ring, extending downward and medially onto the upper part of the scrotum. The left cord was identified and freed. By blunt dissection the left testis and epididymis and tunica were freed and delivered through the wound. The tunica vaginalis was then punctured with a hypodermic needle, a few centimeters of bloody fluid being obtained. The tunica vaginalis was then opened from the upper to the lower pole of the testis. The tunica contained partly liquefied blood clots. The epididymis was found to be black in color, completely separated from the testis, and completely lacking in any blood supply. The testis itself was dark brown-red in color and appeared to have lost the greater proportion of its blood supply. Orchiectomy, left (complete), was carried out (Fig. 1).

The child developed an abscess in the left side of the scrotum on the eighth postoperative day. Aspiration of the abscess yielded 2 cubic centimeters of thick pus mixed with blood. On culture staphylococci were obtained. The upper angle of the wound was opened to provide adequate drainage. The child remained afebrile throughout this period and continued to gain weight from 3,530 grams on the day of operation to 3,800 grams on the tenth postoperative day. He was discharged from the hospital on the eighteenth postoperative day, completely well, and with the wound completely healed.

**Pathology** The specimen consists of a membrane-like sac which has been partially opened, within which two hemorrhagic masses are noted. They are said to represent the tunica vaginalis, the contained epididymis, and the testicle. The spermatic cord is seen entering the tunica. The tunica itself is quite thickened, is red, and quite tough.



Fig.

Fig. Case 1. Photograph of surgical specimen, left testis, epididymis and cord, incised longitudinally showing hemorrhage into testis, with tunica albuginea filled with blood clot.



Fig. 2.

Fig. 2. Case 1. Photomicrograph of portion of testis showing necrosis of central portion. X 5.

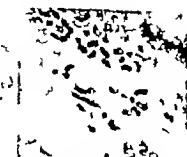


Fig. 3.

Fig. 3. Case 1. Photomicrograph showing degenerated tubules, with hemorrhage. X 40.

There is a folded fibrous band at the upper margin of the epididymis. The epididymis is an enlarged brown-red viscous mass, which is very friable. On section, the entire organ appears to be markedly congested with early signs of necrosis. The testicle is a deep brown-red, quite soft and juicy and tears readily. Sections were taken of the cord, the tunica and the fibrous band per of the epididymis, the epididymis and of the testicle.

The sections of the testicle reveal almost complete necrosis of the entire organ, the central portion being replaced by fibrin, red blood cells, occasional polymorphonuclear leucocytes and necrotic debris. In some areas, remnants suggestive of seminiferous tubules are noted. Similarly in the sections taken through the epididymis there is marked necrosis and hemorrhagic infiltration of the entire section. Occasional tubules are noted which are recognized as such. In the section taken through the spermatic cord, the vas deferens is intact. The accompanying vessels are congested. There is no evidence of any thrombosis.

Diagnosis: Infarction of the left testicle and epididymis. L.L.W. (Figs. 1 and 2.)

CASE. Hospital N. B. 1451. Baby F was admitted to hospital October 30, 1931. The mother

quadrigravida tripara. This pregnancy was normal full term pregnancy. The mother as delivered at home. Delivery as spontaneous, at occiput anterior without instrumentation. The cord was around the baby's neck. The baby breathed with moderate stimulation being cry, moved freely, short time. The birth weight as 91 pounds. The time of delivery the scrotum was noted to be markedly edematous. It was thought that there was enlargement of the testicles.

On the third day of life the baby was examined at home by the pediatric staff members in its regular follow-up of babies delivered on the outside obstetrical service. At this time the whole scrotum was found to be edematous, and showed large areas of bluish-green discoloration, which had increased since birth. The left testicle normal in size, right side of the scrotum, there was an egg-shaped mass measuring approximately 1 1/2 by 3 centimeters. It was freely movable with the scrotum, and adherent to it. The mass was stony hard in consistency.



Fig. 4.

Fig. 4. Case 1. Photograph of surgical specimen showing discolored mass containing testis and tunica vaginalis.



Fig. 5.

Fig. 5. Case 1. Photomicrograph of testicle showing tunica albuginea enclosing organized blood clot and complete



Fig. 6.

degeneration of testicular tissue, with atrophic seminiferous tubules infiltrated with blood. X 5.

Fig. 6. Case 1. Photomicrograph of cord, with vessels free from thrombosis. X 40.

tency Posteriorly, the epididymis could be differentiated from the testis in the upper portion only. The mass did not transilluminate. The right cord was thickened and firm. The child was admitted to the New Haven Hospital on the third day of life, on the pediatric service, under the supervision of Dr Grover C Powers.

Laboratory examinations revealed Kahn test, negative, blood group A, hemoglobin, 18 grams, red blood cells, 5,160,000, white blood cells 9,850, differential white blood cell count—polymorphonuclear leucocytes 40 per cent, lymphocytes 46 per cent, large monocytes 9 per cent, blood platelets, normal, bleeding time,  $1\frac{1}{2}$  minutes, clotting time,  $2\frac{1}{4}$  minutes, urine examination, normal, Aschheim-Zondek test, negative, x ray of chest, normal, enlarged thymus noted.

A urological consultation was requested on the fourth day of life. The patient was observed daily by the members of the urological staff during the next 5 days, during which time the child remained afebrile. He was given formula feedings, and gained in weight from 4,600 grams to 4,700 grams. During this period the edema of the scrotum diminished, the areas of ecchymosis remained unchanged in size, but became deeper in color. The mass in the right side of the scrotum did not change in size or consistency. A diagnosis of hemorrhage into the right testicle was made. On the tenth day of life, exploration of the right scrotal sac was carried out.

A skin incision was made over the right external inguinal ring and extended downward, forward, and medially onto the upper portion of the scrotum. By blunt dissection the cord was freed, and the mass in the right side of the scrotum delivered into the wound. When the tunica vaginalis was opened, about 15 cubic centimeters of amber colored fluid escaped. Cultures were taken. These were later reported as showing no growth. The testis and epididymis appeared as a mass of grayish black necrotic tissue. Orchidectomy, right, and epididymectomy, right, were carried out. An elastic band was inserted as a drain through a stab wound in the dependant portion of the scrotum (Fig. 4).

Recovery was entirely uneventful, the child remaining afebrile throughout, and gaining in weight from 4,700 grams at the time of operation to 5,180 grams at the time of discharge on the fourteenth postoperative day.

**Pathology** This specimen consists of the distal portion of a spermatic cord, the epididymis, testicle, and opened tunica vaginalis. At the junction of the spermatic cord in the epididymis there is a fusion of all the elements of the cord, and a rounded tight knot of soft tissue, the outermost coat of which consists of tunica vaginalis. There seems to be a natural constriction at this point. Distal to this, the tunica vaginalis is not remarkable. The testicle measures 4 centimeters in its longest diameter. When it is opened, it is seen to consist of a uniform deep brown colored tissue. The seminiferous tubules string with ease. Within the tunica albuginea, and distinct from

the testicle, there is an encapsulated mass of soft tissue, which also appears to contain tubules. This is in no place continuous with the testicle proper. This too is of the same deep brown color as the testicle. The epididymis is present, and is not remarkable other than showing the uniform brown color. On cut section through the junction of the tunica vaginalis with the other elements of the cord, at the point of constriction, the vas is identifiable. The vessels are not distinct, but are fused together to form a uniformly brown tubular structure which apparently is thrombosed. This structure is about 3 centimeters in diameter. Representative sections were taken from the testicle, and the adjacent mass, as well as from the cord, for microscopic study.

In the sections of the testicle, a diffuse infarct is noted, involving all of the structures contained within the testicle, the epididymis, and its covering. There is evidence of old hemorrhage and beginning organization scattered throughout all portions on the slide. The epididymis is characterized by a similar process. In the section of the testicle, some of the vessels noted show evidence of calcium deposits within their walls. There is no evidence of any organizing thrombi. In the sections of the spermatic cord, the vessels are congested. There is no evidence of any obliteration of the lumina of these vessels. The spermatic cord and the vas deferens are present, and are not remarkable.

**Diagnosis** Hemorrhagic infarct in right testis and epididymis, with beginning organization, calcium deposits within the intrinsic vessels of the spermatic cord. H B (Figs 5 and 6).

Hernia, hydrocele, epididymitis, tumor of the testicle, torsion of the testicle, and torsion of the appendix testis must be considered in the differential diagnosis of hemorrhagic infarct of the testis in the newborn. Hernia usually gives little difficulty in the diagnosis. It gives the characteristic impulse on coughing, is resonant on percussion, and when it contains bowel, gurgles on being reduced. A hydrocele has an elastic cystic feel to it, and transmits light. An acute epididymitis is invariably accompanied by severe pain and fever. There is no pain associated with hemorrhagic infarct of the testicle in the newborn, and the patient is afebrile.

Tumor of the testicle is nearly always stony hard in consistency. In these 2 cases of hemorrhagic infarct, the mass was stony hard in one, and fibroelastic in the other. In both cases, the ecchymosis in the scrotum provided sufficient evidence to eliminate tumor of the testis.

Torsion of the testicle and torsion of the appendix testis must be excluded. In both of



these, the onset of acute unilateral pain is practically always sudden. In torsion of the appendix testis there is a concomitant redness and edema of the scrotum at the onset of the attack and in children there is a slight elevation of temperature. In cases of a few days duration, unless edema persists or a secondary hydrocele interferes, spot tenderness at the superior pole of the testis, and just under the globus major of the epididymis is diagnostic (Randall). In torsion of the testicle Preen's sign is present. In hemorrhagic infarct of the testicle the testicle can be palpated freely without the child showing any signs of discomfort. Figure 6 shows a cross section of the spermatic cord in Case 2. It will be seen that the vessels are entirely free from thrombosis.

A diagnosis is made by the presence at birth of a mass within the scrotum the mass is usually egg shaped and may be fibroelastic or stony hard in consistency the presence of ecchymosis of the scrotum and the absence of pain or tenderness in the affected testicle Preen's sign is absent and the patient is afebrile. The white blood cell count may be slightly or moderately elevated, the red blood cell count remains normal.

#### CONCLUSIONS

1. Two cases of hemorrhagic infarct of the testicle in the newborn are presented.
2. In both cases the delivery was normal and uncomplicated.
3. A diagnosis is made by the presence at birth of a mass within the scrotum the presence of ecchymosis of the scrotum absence of pain absence of Preen's sign a normal temperature and a slightly elevated white blood cell count.
4. Hernia, hydrocele epididymitis, tumor of the testicle torsion of the testicle and torsion of the appendix testis must be considered in the differential diagnosis.
5. Torsion of the spermatic cord was not present in either case.
6. Orchiectomy was done in both cases, recovery being uneventful.

#### REFERENCES

1. CAMPBELL, MENDENHALL. *Pediatric Urology* Vol. 2, pp. 87-183, New York, Macmillan & Co. 1917.
2. CEDERHJELM, J. *Acta chir. scand.* 1916, 73: 417-444.
3. CORLIAC, J. *Urol. Balt.*, 1914, 31: 904-907.
4. LEVINE, S. *J. Urol. Balt.*, 1917, 34: 1-3.
5. MENDENHALL, JOHN O. *J. Urol. Balt.* 1911, 41: 317-318.
6. NELSON, C. E. *Practitioner*, 1919, 95: 497-499.
7. ODELL, H., and S. W. K. *J. Endocr.* Oct., 1924, 10: 279.
8. RANDALL, ALEXANDER, T. *Am. J. Gynecol.* 1913, 3: 283-294.

# THE IMMEDIATE EFFECTS OF 3,3'-METHYLENEBIS (4-HYDROXYCOUMARIN) ON EXPERIMENTAL ANIMALS

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IN a series of publications, Link and his associates (5, 9, 20) successfully showed the isolation, identification, and later synthesis of the hemorrhagic principle from spoiled sweet clover which has been responsible for the "sweet clover disease" of cattle (15, 16, 18). The substance is chemically 3,3'-methylenebis (4-hydroxycoumarin), and has the abbreviated name of dicumarol.<sup>1</sup> The economy of its manufacture by synthetic methods, the effectiveness by mouth, and the possibility of replacing heparin in preventing thrombosis, have attracted the attention of both experimental and clinical investigators. Published reports (1, 3, 4, 12, 21) indicate that in both animals and men, hypoprothrombinemia resulting from the administration of dicumarol requires a latent period of about a day. The peak of action may occur on the third day after a single dose. The prevention of the formation of thrombi can be demonstrated in dogs receiving dicumarol, thus providing the basis for clinical trials to prevent thrombosis (6, 14). A few preliminary papers on this point have appeared (7, 10, 11, 19, 22).

In animals which have succumbed to lethal doses, hemorrhage into various tissues and organs is an outstanding feature (3, 17). The liver of the rat is relatively more susceptible to dicumarol, often showing central necrosis after continuous administration (17). Dilatation of capillaries, small arteries, and veins has been observed in those animals that die acutely from massive doses (3). Other terminal effects, which have been recorded, include fever, dyspnea, coma (3) and convulsions (17). It is possible for dicumarol to kill animals within a few hours (17).

The purpose of the present communication is to report various results observed by us

during the early stages of intoxication by dicumarol—prior to the onset of hypoprothrombinemia. In practically every experiment, a lethal dose was employed. The data deserve emphasis because they may not involve the same mechanism which determines the changes of prothrombin level.

## METHODS

Dogs, rabbits, and albino rats were used in this study. The dogs were anesthetized with ether and the blood pressure was recorded from the carotid artery by means of a mercury manometer. Sodium citrate was employed to prevent coagulation of the blood in the arterial cannula. The respiration was recorded with a tambour connected to the side arm of the tracheal cannula. A 0.5 per cent solution of the disodium salt of dicumarol prepared according to Link's directions (private communication) was administered into the femoral vein. Before and after the dicumarol injections, the prothrombin time and the coagulation time were taken at intervals throughout each experiment. The individual doses injected ranged between 5 and 15 milligrams of dicumarol per kilogram of body weight.

For direct study of the behavior of the vascular system under the influence of dicumarol, albino rats anesthetized with ether or with pentobarbital sodium were used. Dicumarol in 0.5 per cent solution was injected into the femoral vein and its acute effects on the vascular bed were studied *in vivo* by the quartz rod transillumination technique. Precautions to prevent chilling of the animal were taken by placing the rat on a constant temperature platform (23).

The prothrombin time of diluted and undiluted plasma was determined by the Quick technique modified by Pohle and Stewart. A volume of 1.8 cubic centimeters of blood was

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<sup>1</sup>Dicumarol is the collective trade mark of the Wisconsin Alumni Research Foundation which controls the use thereof.

withdrawn into a syringe containing 0.2 cubic centimeter of 0.1 mol sodium oxalate solution and then centrifuged.

The coagulation time was determined by the capillary tube method, and the red cell count made according to routine procedures.

### RESULTS

The intravenous administration of 5 to 10 milligrams of dicumarol per kilogram of body weight in the form of a 0.5 per cent solution of dicumarol into anesthetized dogs brought about slight but transient fall in blood pressure and occasionally a slight increase in amplitude of respiration. However when the total quantity administered amounted to between 40 and 60 milligrams of dicumarol per kilogram of body weight the respiration became very rapid and irregular and was followed by severe dyspnea. In spite of the rapid and deep respiration the blood became darker and darker as time went on. Cardiac irregularities, in the form of extra systoles showed up in some of the animals. Hyperpyrexia became quite evident and the animal's temperature rose from an average of 38.5 degrees C. to as high as 42 degrees C. by the end of the experiment which invariably lasted less than 1 hour. A generalized vasodilatation was manifested and the heart action and respiration stopped simultaneously resulting in death of the animal within 1 hour from the very start of the experiment. There was no change in the prothrombin or coagulation times throughout all the experiments. A slight rise of the red cell count was observed. Immediate postmortem examination showed a very dark and congested liver, an extremely contracted spleen, and very dark blood with general vasodilatation throughout the visceral and peripheral vessel beds. The onset of rigor mortis was immediate, and the animals became stiff soon after death. The findings under the influence of intravenously administered dicumarol may be summarized as follows:

(1) Rapid irregular respiration followed by severe dyspnea (2) generalized vasodilatation (3) extreme darkening of blood, in spite of rapid and deep respiration (4) cardiac irregularities extra systoles (5) hyperglycemia (6) hyperpyrexia—temperature rose from 38.5

TABLE I—LETHAL DOSES OF DICUMAROL IN ANESTHETIZED DOGS

Dog Number	Intravenous dose mgm. per kgm.	Total amount administered mgm.	Result
	45	252	Died after 30 minutes
	25	45.5	Died after 25 minutes
	20	66	Died after 25 minutes
	25	66	Died after 45 min.
	60	100	Died after minutes
	20	200	Died after 30 minutes
T	20	250	Died after 45 minutes
Controls			
64	24.00 C.C.	480 C.C.	No effect
30	24.25 C.C.	470 C.C.	No effect

degrees C. to 42 degrees C. (7) hypermetabolism (8) heart action and respiration stopped simultaneously (9) liver very dark and congested (10) spleen extremely contracted (11) coagulation and prothrombin times did not change throughout the experiment (12) slight hemoconcentration (13) the animals became stiff immediately after death.

In order to determine whether or not any of the other ingredients of the dicumarol solution had any effect on the animals, control solutions were made incorporating all the ingredients exclusive of dicumarol. A total of 260 cubic centimeters of this control solution was given to one normal dog, and a total of 230 cubic centimeters to another. Neither of the control animals showed any toxic effects. It was justifiable therefore to conclude that the aforementioned manifestations were due to the dicumarol administered in the solution. Table I gives the dosages of dicumarol and of the control solutions per kilogram of body weight and per animal and indicates their outcome. It should be noted that all the experimental dogs died within 1 hour and showed the findings as here listed while the controls were not at all affected by a solution containing all the ingredients except dicumarol.

The *in vivo* study of the vascular bed in the anesthetized albino rat by the quartz rod transillumination technique demonstrated a generalized dilatation of the small vessels of the splanchnic area. No damage to vessel walls, however, could be observed.

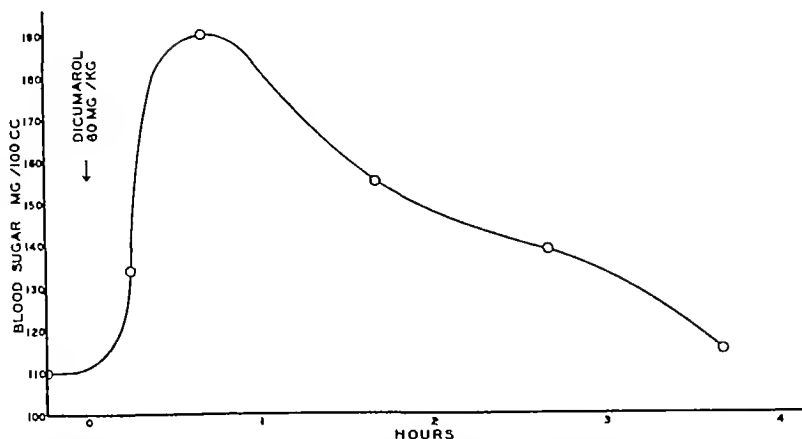


Fig 1 Hyperglycemic action of dicumarol Rabbit, male, weighing 2.13 kilograms, was given by the marginal ear vein dicumarol in the dose of 60 milligrams per kilogram Note the rise of blood sugar from 110 to 190 milligrams per 100 cubic centimeters in 40 minutes

Since hyperpyrexia was consistently observed in anesthetized dogs under the influence of intravenously administered dicumarol, we were interested in finding out whether or not it would raise the temperature of the conscious animal. Five trained dogs were used and every one developed hyperpyrexia when the drug was given intravenously in the dose of 50 to 60 milligrams per kilogram. We were further interested in finding out whether or not dicumarol would produce a rise of temperature in the rat when administered orally. A dose of 700 milligrams per kilogram was administered orally to a group of 4 rats, one of 900 milligrams per kilogram to another group of 5 rats, and one of 1000 milligrams per kilogram to a third group of 5 rats. Their rectal temperature was recorded hourly with a thermocouple and a definite rise of temperature was obtained.

In view of the hyperpyretic action of dicumarol, an acceleration of metabolism was suspected. Twelve rats were given dicumarol orally in the dose of 700 milligrams per kilogram, and their metabolic rates were measured in a Benedict's multiple chamber respiration apparatus (2). There was a uniform increase of metabolic rate: on the average, 119 per cent during the first hour after the medication, 202 per cent during the second hour, and 229 per cent during the third hour, as compared with the initial rate, namely, im-

mediately before the medication. Five animals died before the end of the third hour.

To determine whether or not dicumarol has any effect on blood sugar, rabbits were given doses of 50 to 60 milligrams per kilogram intravenously. Their blood sugar was determined by the Hagedorn-Jensen method (8). There was definite evidence of hyperglycemia with prompt recovery. Figure 1 shows an example of the effect of intravenously administered dicumarol on the blood sugar of a rabbit.

#### ANALYSIS OF STUDY

Heretofore, dicumarol has been known to reduce, after a prolonged latent period, prothrombin levels of experimental animals. When the dose is excessive or frequently repeated, hypoprothrombinemia leads to severe hemorrhages and death. The results from the present investigation are interesting, particularly because they appeared promptly after the administration of dicumarol. It is probable that their occurrence is not associated with the same mechanism which controls the changes of prothrombin time. The sudden circulatory collapse in dogs suggests the acute dilatation of the capillaries and small vessels due to the drug, which has already been observed in the visceral organs. The direct action on the heart has not been excluded. The increase of metabolic rate and the rise in rectal tempera-

ture constitute another side action. Either circulatory collapse simulating shock or hyperpyrexia may be the cause of the very acute death in animals. The brief hyperglycemic effect cannot be explained without further elaborate studies of carbohydrate metabolism under the influence of dicumarol.

It must be pointed out that the above results were observed with lethal doses in animals. They have no clinical application when therapeutic doses are employed in men. The only place where these toxic manifestations may be kept in mind is in cases of poisoning accidental or otherwise by unusually large amounts of dicumarol.

#### SUMMARY

1 Intravenous injection of lethal doses of dicumarol to anesthetized dogs results promptly in a series of toxic manifestations including terminal circulatory collapse—with out evidence of hypoprothrombinemia. No latent period of reaction is required.

2 Lethal doses of dicumarol injected intravenously to anesthetized rats cause splanchnic vasodilatation as shown by the quartz rod transillumination.

3 Hyperglycemia in rabbits, acceleration of metabolic rate in rats and rise of rectal temperature in both dogs and rats, have been consistently observed shortly following the lethal doses of dicumarol.

#### REFERENCES

- BARKER, V. W., BUTT, H. R., ALLEN, E. V. and BOLDWIN, J. L. *J. Am. M. Ass.*, 942, 1 1003.
- BYRONICK, G. J. *N. Y. J. Biol. Sci.*, 930, 1 10.
- BINGHAM, J. B., MEYER, O. U. and FOWLE, F. J. *Am. J. M. Sc.*, 94, 80 303.
- BUTT, H. R., ALLEN, E. V. and BOLDWIN, J. L. *Proc. Mayo Clin.*, 94, 6 378.
- CAMPBELL, H. A. and LING, K. F. *J. Biol. Chem.*, 94, 38 379.
- DALE, D. U. and JACOBS, L. R. *Canad. M. Ass. J.*, 942, 60 546.
- F. V. A. *Labor. Clin. Bull.*, 942, 7 117.
- HAGDON, H. C. and JENSEN, R. V. *Archiv. Zool.*, 923, 33 46.
- HUTCHINSON, C. F. and LING, K. F. *J. Biol. Chem.*, 94, 38 379.
- LEHMANN, J. *Lancet, Lond.*, 942, 318.
- MEYER, O. U., BINGHAM, J. B. and ALLEN, E. V. *Am. J. M. Sc.*, 942, 8041, 2.
- MEYER, O. U., BINGHAM, J. B. and FOWLE, F. J. *J. Am. M. Ass.*, 942, 8 1003.
- FOWLE, F. J. and STEWART, J. K. *Am. J. M. Sc.*, 94, 6 2.
- RICHARDS, R. K. and CORTELLI, R. *Proc. Soc. Exp. Biol.*, 94, 50 37.
- RODRIGUEZ, L. M. *J. Am. Vet. M. Ass.*, 939, 37 11.
- Idem. *Am. J. Physiol.*, 93, 66 43.
- ROD, C. L., HILARY, P. V. and CHEN, K. K. *Proc. Soc. Exp. Biol.*, 94, 50 37.
- SCHWETZ, J. W. *J. Am. Vet. M. Ass.*, 944, 7 551.
- SCHWETZ, S., SCHWETZ, R., RICHARDS, M. and CAMPBELL, H. A. *Proc. Soc. Exp. Biol.*, 94, 50 37.
- SARIN, V. M. V. HUTCHINSON, C. F. and LING, K. F. *J. Biol. Chem.*, 94, 38 379.
- TH. D. and BULLOW, J. G. M. *Proc. Soc. Exp. Biol.*, 94, 50 37.
- TH. D., S. R. and MILLER, E. S. *Canad. M. Ass. J.*, 942, 46 1.
- W. L. R. O. and M. V. C. *Arch. Rec.*, 942, 33.



TABLE I—EFFECT OF EXTENT OF AXILLARY METASTASES ON SURVIVAL

	No. cases	Living and well 5 years or over	Living and well 3-4 years	Average survival of cases dead with disease less than 3 years
No metastases to axillary lymph nodes	4	3	1 <sup>b</sup>	2
Metastases involving less than half the axillary lymph nodes			30	
Metastases involving more than half the axillary lymph nodes		15		
Metastases involving 75% of the axillary lymph nodes	27	14	14	
Total with metastases to axillary lymph nodes	31		28	
Total	171	34	39	2

evident. On the other hand we have included 1 patient as a cure who died only 4 years after operation, because autopsy failed to reveal any evidence of cancer. Ten patients were called cures at the time of death from intercurrent disease 6 to 10 years after operation because they had been observed by us frequently during the course of that time and had remained free of cancer. Nine of these were aged the tenth, a 26 year old woman died of rheumatic heart disease 7 years after operation and was found to be free of tumor at autopsy. Patients living with recurrences at the time of this study were included as dead. Otherwise the results are expressed in terms of 5 to 13 year survival free of disease on clinical examination. In this respect it is comparable rather to Summons' series than to the conventional 5 year cure. In Table I 5 year cures are also tabulated for comparison.

A fairly large number of cases was not considered suitable for study because the axillary contents had been lost or we had reason to believe that not all the axillary lymph nodes had been prepared for histological examination. This group occurred chiefly in the early years of the hospital before there was a standard procedure for examining the axillary contents.

The primary tumors were classified according to their microscopic characteristics as carcinoma simplex, adenocarcinoma, and mucinous carcinoma. Histological grading of carci-

noma of the breast has not been found significant in this laboratory. The axillary contents were carefully examined and all the lymph nodes found were studied histologically. Colfer has shown that by clearing techniques a substantially greater number of lymph nodes are discovered than by the usual methods and that metastases occasionally occur in the small easily overlooked nodes. We have used only careful dissection and palpation of the axillary tissues.

One might question the validity of dealing with the number or percentage of involved nodes as we have done without knowing their relative positions in the axilla. This criticism is somewhat offset by the fact that a group without metastatic nodes or a group with all the nodes tumorous would be unaffected by any such means of classification. In our series only a single section was prepared of a given lymph node in most instances. While we realize that clearing techniques, serial sectioning, and the keying of nodes of basal, middle, and apical axillary groups might give more accurate data, these methods are time consuming, expensive and generally unsuited to routine laboratory use. The method we have used is feasible in any pathology laboratory and as such has its advantages.

## RESULTS

*Effect of extent of axillary metastases.* The 171 patients are divisible into four groups: namely without lymph node metastases with metastases involving less than half the lymph nodes, with metastases involving more than half the lymph nodes, and with metastases involving all the lymph nodes. Further subdivision is possible and gives results in keeping with the general trend, but the groups are too small to be of statistical significance.

The most significant finding is that curability on the basis of 5 year cure or longer periods of observation is inversely proportional to the extent of metastasis in the axilla (Table I). Fifty per cent cure in the group with least axillary involvement and 16 per cent cure in the group with most axillary involvement varies significantly from the average cure rate of 28 per cent for the whole group with axillary metastases. The time of

survival in the fatal cases is also longer in the less involved group than in those more heavily involved. It is apparent, therefore, that the consideration of the whole group as homogeneous is ill advised. This is especially important to consider when small series such as this are studied for the purpose of judging the operation of some variable. An example of this will be dealt with later in this paper under the subject of recurrences in the operative scar.

The poor prognosis generally given the case with a few axillary metastases is probably unjustified. Although our data are insufficient to establish the point, we have gained the impression that patients with metastases to only one or two of a dozen or so axillary lymph nodes have nearly as great a chance of cure as those without such metastases. Moreover, patients with most or all of their axillary nodes involved by tumor not only have a much poorer prognosis for life but survive a shorter period than do those with less extensive metastases. The data on survival of the various groups are shown in Table I and are presented graphically in Figure 1.

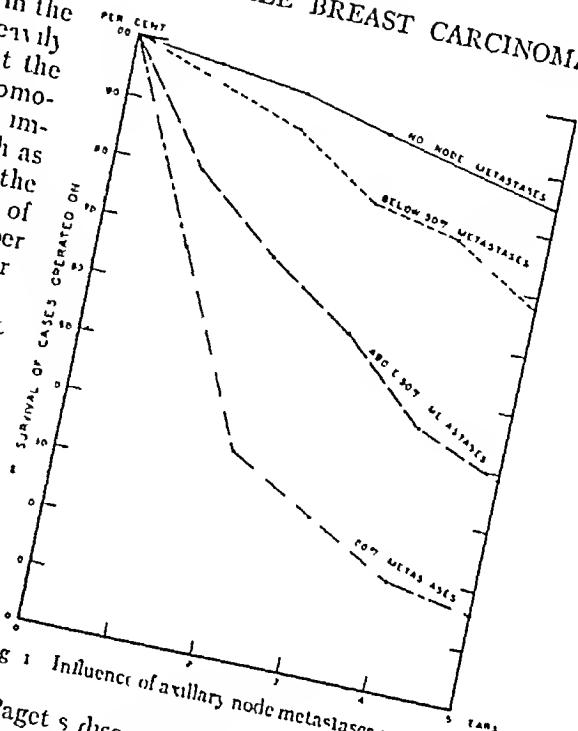


Fig 1 Influence of axillary node metastases on survival

Paget's disease of the nipple occurred in 4 patients. Three with metastases to lymph nodes are dead, the fourth with no lymph node metastasis is cured.

Adenocarcinoma occurred without lymph node metastases in 11 patients. Eight of these are cured. Four patients with the same type of tumor had node metastases and 2 of these are cured.

The majority of the tumors were classified as carcinoma simplex, and in these the results parallel the figures of the groups as a whole. This is a small series on which to base conclusions, but it would seem that the type of tumor has less significance in prognosis than its extent.

We made no effort to grade the primary tumors according to the method of Broders. We do not ordinarily grade breast cancers because we believe the personal equation in the process to be very great, particularly as regards the intermediate grades, and we have found the results not significant. Variation in the grade of malignancy of these cases may account for some of our case distribution as regards metastases but cannot invalidate our principal conclusions.

The periods of time elapsed between operation and death in those who died of cancer in this series give further data. Seventy-seven per cent of those with all their lymph nodes involved were dead in 2 years whereas only 20 per cent of those with less than half their nodes involved died in a similar time. In the group without axillary node metastases we found, as did Simmons, that the patients who survived 5 years without recurrence may be considered permanent cures.

**Effect of type of primary carcinoma.** Mucinous (gelatinous or colloid) carcinoma or adenocarcinoma with mucinous foci was encountered in 5 patients in this series. Four showed no lymph node metastases, 1 had metastases to a third of the axillary nodes, which fact placed her in the lowest division of cases with lymph node involvement. All 5 of these patients are cured.

Carcinoma originating in papillary cystadenoma occurred in 7 patients. Six of these had no axillary metastases, 4 are cured. The seventh had all her axillary nodes involved and she is dead of cancer.



TABLE II —RELATION OF LYMPH NODE METASTASES TO RECURRENCES IN THE OPERATIVE SCAR

Number of cases	Metastases to axillary lymph nodes Per cent	Recurrences in operative scar Per cent
8	under 50	7
1	over 50	9
37	00	0

*Recurrences in the operative scar* The data bearing on this point are presented in Table II. It is apparent that for this series at least recurrences in the operative scar increase with the extent of the disease in the axillary lymph nodes. It is reasonable to suppose that patients in whom metastases have occurred to axillary nodes should also have other metastases to the skin or the chest wall thus increasing the likelihood of recurrence in the scar. We believe the data support this supposition. The grave prognostic significance of such recurrences is seen in the group of patients in whom the lymph nodes were uninvolvement. All the patients in this group who developed recurrences in the operative scar died of cancer. Of the 19 patients in the same group who died of cancer 6 developed recurrences in the operative scar. In the group with axillary metastases only 2 of the 16 patients with recurrences in the scar were cured.

The incidence of recurrences in operative scars suggests that they are of the nature of

metastases or extensions rather than implants. We believe that the variation of this type of recurrence in the reported series may be explained by differences in the type of cases treated and that this ought to be taken into account before deciding on the effect of changes or improvements in surgical technique.

#### SUMMARY AND CONCLUSIONS

The extent of involvement of axillary lymph nodes was studied in 171 cases of carcinoma of the female breast treated by radical mastectomy. Curability, as well as the survival time of patients not cured, decreases as the extent of metastases to the axillary lymph nodes increases. Recurrence in the operative scar is more apt to occur as the extent of axillary involvement increases.

Patients with metastases to the axillary lymph nodes do not form a homogeneous group and there is prognostic value in further subdividing them. With such subdivisions the study of cases is made more accurate even in small series, and the prognosis in a given case can be made with a little more assurance.

#### REFERENCES

- COLLIER, F. A., KA, E. B. and McFETTER, R. S.  
Surgery, 640, 3: 307-311
- SCHWENK, C. C., TILSON, G. W. and WELCH, C. L.  
Surg. Gyn. Obst., 930, 69: 71-77
- TILSON, G. W. and BATES, N. H. N. England J.M.  
940, 790-792

# "SHOCK" AND ANESTHESIA IN TRANSTHORACIC GASTRIC SURGERY

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## MATERIAL AND METHOD OF STUDY

The material for this study was drawn entirely from the clinic. The problem has been approached chiefly through examination of the circulatory effects of the two routes of approach. It has been demonstrated that careful observation of the trend of the patient's systolic and diastolic blood pressure, pulse rate and quality, the skin circulation rate and skin temperature, blood color, and in some cases type and rate of respiration is useful in estimating the status of a patient at any given time and in predicting his course during operation. When one couples with these simple observations further objective data concerning the patients' circulatory stability during the immediate post-operative period and the character and duration of his recovery period in general, it becomes possible to state with considerable certainty whether one procedure is tolerated on the average as well or better than another. These matters are routinely followed in this clinic and notes are made concerning them. The patients of the two groups receive equivalent care, transfusions when needed and oxygen.

For brevity, specific data (Table I) are presented concerning only systolic and diastolic pressures and pulse rate, since in these patients breathing oxygen rich atmospheres with adequate respiratory minute volume the other factors mentioned were satisfactory unless the contrary is specifically stated. In Table II the circulatory effects observed under the five methods of anesthesia customarily used for anesthesia in this hospital for gastric resection are recorded, the same number of cases being considered in the average for each group.

## ANALYSIS OF STUDY

While the average data with the standard errors of the mean (Table I) give a good over-all picture additional information is important. In the case of the transabdominal wall surgery (either) only 1 (5, years of age) patient's systolic blood pressure

THE point of view has persisted generally that only the robust are likely to withstand transpleural surgery. What truth there may be in this generalization remains to be shown, however, at this time enough material is at hand to permit an objective test of the matter, although of course the conclusions reached must remain tentative until a large body of material accumulates. Good material for examination in poor risk patients can be found in the group of patients who have carcinoma of the stomach. This lesion, approached by transabdominal wall route as well as by transpleural route for anatomical reasons, has now been operated on enough times through the latter entrance to permit study and comparison of the shock producing effects of the two approaches. The material considered here is divided as follows: 64 patients with resectable carcinoma of the stomach have been studied, 17 of these have undergone gastric resection through the pleura and 17 by the traditional route, both of these groups were under either anesthesia, and for comparison 30 patients have had gastric resection under spinal or splanchnic block or local anesthesia through the latter route. From present experience it seems clear that the transpleural approach may in fact produce no more shock and perhaps even less than the transabdominal wall approach to the stomach. Thus, in addition to compelling anatomical reasons for approaching certain upper abdominal lesions through the thorax, the surgeon may be supported by a further fact. The excellent operative tolerance of the patient for the transpleural approach. The principles and procedures of anesthesia which are important in transpleural abdominal surgery will be discussed, and in this connection probable reasons for the excellent tolerance of patients for the transpleural approach to the upper abdomen will be considered. And finally to be discussed are some lessons that have been learned from civilian thoracic surgery and anesthesia that are of importance in the care of war injuries of the chest.

From the Anesthesia Laboratory of the Harvard Medical School and the Anesthesia Service at the Massachusetts General Hospital.  
Manuscript received for publication May 1, 1941.  
Presented at the Annual Meeting of the American Society of Anesthesiologists, New York, N. Y., 1941.  
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TABLE I—THIRTY FOUR GASTRIC RESECTIONS FOR CARCINOMA UNDER ETHER ANESTHESIA  
A series with Standard Errors of the Means

## SEVENTEEN CONSECUTIVE TRANSABDOMINAL WALL APPROACHES

Age $\pm$ 1	Sex	M	F	Duration of procedure	hours, minutes $\pm$ 5 minutes
	A. entry to hospital			After hours of anesthesia and operation	After hours of anesthesia and operation
Blood pressure and pulse rate	Systolic Diastolic Pulse	$\pm$		$\pm$	$\pm$
				78 50 104 $\pm$ 3	75 50 104 $\pm$ 3

## SEVENTEEN CONSECUTIVE TRANSPLEURAL APPROACHES

Age $\pm$ 1	Sex	M	F	Duration of procedure	hours, minutes $\pm$ 5 minutes
	A. entry to hospital			After hours of anesthesia and operation	After hours of anesthesia and operation
Blood pressure and pulse rate	Systolic Diastolic Pulse	$\pm$		$\pm$	$\pm$
				78 50 104 $\pm$ 3	75 50 104 $\pm$ 3

fell below 80 millimeters mercury. In this case the blood pressure had declined to 65/40 with a pulse rate of 120 at the end of operation 2 hours and 50 minutes after the beginning of anesthesia. The patient was described as in poor condition with considerable surgical shock.

In the case of the transpleural surgery (ether) the blood pressure of a patient (68 years of age) slowly and gradually declined and at the end of operation, 3 hours and 50 minutes after anesthesia had started, had fallen to 78/50, with a pulse rate of 100. Other signs of shock did not develop and the patient was described as standing the operation well. Immediately following operation the blood pressure rose to 92/60 and then rapidly returned to normal. Another patient (36 years of age) showed a steady, gradual decline of blood pressure to 73/40, with pulse rate of 125 at the end of operation 4 hours and 10 minutes after the start of anesthesia. Other signs of shock did not develop. By the end of 1 hour following operation the blood pressure had risen to 100/60.

The pulse rate had fallen to 100. The blood pressure promptly returned to normal. A third case in this group illustrated in a striking way the excellent tolerance of patients for this approach. The patient was a 75 year old man with carcinoma involving the esophagogastric junction. While on the ward, the patient's lesion began to bleed suddenly and with continued hemorrhage over period of several hours, his blood pressure fell to 70/40 with typical signs of profound shock. He was in shock when the anesthesia was started. His blood pressure rose during the transthoracic gastric resection which included splenectomy and partial pancreatectomy. At the end of the procedure the patient's blood pressure had risen to

110/84 with a pulse rate of 108, his skin was warm and dry and his color good. Rapid recovery from shock took place notwithstanding the another and transpleural operation and also despite a 14 hour period of difficulty in getting a transfusion started during the operation.

Briefly then a patient in the transabdominal wall group (ether) developed shock as a result of the anesthesia and operation. In the transpleural group no patients developed shock although there were 2 instances of low blood pressure after these procedures. Another patient in both shock had developed before anesthesia and operation was started recovered from shock during the transthoracic procedure. As far as these data go, both procedures are well tolerated.

The data Table I cannot be considered in any precise mathematical way; there are too few they do afford however a useful sample of a large body of information of which they are typical. Thus during transpleural surgery under ether the relative constancy of the systolic blood pressure, the constancy of the diastolic pressure and the pulse rate are evidence that what we call the patient's circulatory equilibrium is being maintained to a remarkable degree. Since this is despite prolonged, increasingly adverse conditions (surgical trauma, blood loss, heat loss) this must be maintained by active finely balanced compensatory mechanisms. We can generalize from the constancy of the systolic and diastolic pressures and the unchanged pulse rate that the effective cardiac output probably continues unchanged even throughout 4 hours. During these 4 hours we know that the patient is subjected to prolonged deleterious stimuli notwithstanding these evident facts his diastolic pressure per-

TABLE II—FIFTY RECENT GASTRIC RESECTIONS FOR CARCINOMA  
10 Patients in Each Group

Anesthesia	Duration	Patients		At entry	Time following induction							
		Sex M F	Av age		1 hr Blood pressure	Pulse	2 hrs Blood pressure	Pulse	3 hrs. Blood pressure	Pulse	4 hrs Blood pressure	Pulse
Ether Transpleural operation	3 hrs. 59 min	8 2	55 8	119/70	110/73	99	116/78	105	112/77	103	107/73	102
Ether Transabdominal wall operation	2 hrs 54 min	8 2	54 2	131/83	132/76	106	133/80	106	116/72	109		
Spinal Transabdominal wall operation	2 hrs 16 min	7 3	57 7	137/81	109/68	92	109/69	102				
Splanchnic Block Transabdominal wall operation	2 hrs 37 min	6 4	61 1	136/78	111/65	96	125/72	98				
Local Transabdominal wall operation	2 hrs 13 min	7 3	63 2	127/80	104/65	93	106/68	88				

unchanged. Apparently it can only have been maintained unchanged by active processes compensating for the obvious opposing factors (anesthesia, surgical trauma, blood loss). At the end of operation these patients customarily are warm. The skin of the forehead shows a very active capillary circulation as indicated by immediate reflushing of areas blanched by light pressure.<sup>1</sup> The pulse is full and of good quality.

When the resection of the stomach is carried out through the abdominal wall under ether anesthesia, the systolic and diastolic pressures and the pulse rate persist unchanged as presumably the cardiac output does also, active peripheral constriction must have been occurring to oppose the influence of the obvious blood loss and the other deleterious factors, yet after 3 hours of anesthesia and gastric surgery through the abdominal wall in this rather old group with cancer, the typical patient is pale, cool, and sweating, with a pulse of rather poor quality.

Although no significant differences in the systolic or diastolic pressures or the pulse rates of these two groups were observed, it is evident that after 4 hours of gastric surgery through the thorax the general appearance of the patients in this group is better than it is after an even shorter intervention through the abdominal wall. On the basis of the data at hand and the experience to date it appears to be safe to say that gastric surgery through the thorax is no more shock-producing and perhaps even less so than gastric surgery

carried out through the abdominal wall. There are reasons why this should be so. The clearer cut ones can be summarized briefly.

a Gastric surgery through the thorax can be carried out at a far higher level of anesthesia than is possible when the anterior abdominal wall route is used. In the former case relaxation of the abdominal wall is not necessary. The only relaxation needed is that of the diaphragm, and this can be obtained by a drop or two of procaine injected into the phrenic nerve under direct vision.

b When the transabdominal wall route is used, the surgeon is constantly disturbing the large blood vessels and nerve plexuses of the abdominal cavity, he constantly subjects the pedicles of the abdominal organs to pressure or to tension. These actions are well known to produce harmful circulatory effects, and ultimately a fall in blood pressure. There is relatively little disturbance of the intra-abdominal structures adjacent to the stomach in the transpleural approach.

It will also be a matter of great interest to observe, when adequate data have accumulated, if gastric surgery carried out with light anesthesia and without an abdominal incision is followed by a lower incidence of postoperative pulmonary complications than is true following the abdominal incision. There are good reasons for believing that such may prove to be the case.

The evidence suggests that in the hands of a properly qualified operating team, when the gastric lesion is such that it can for anatomical reasons be more easily approached through the transdiaphragmatic route, there is no reason to fear more "shock" with this approach than with the

<sup>1</sup>This is a very useful test for following the decrease in skin circulation which precedes the onset of shock. Normally, reflushing of the skin occurs in a second or less after blanching by light finger pressure. With slowing down of the peripheral circulation an appreciable delay is easily apparent.

traditional transabdominal wall approach. Certainly this is only one aspect of the problem and other possible hazards beyond the scope of this study must be evaluated before the transpleural approach can become standard procedure.

Further data of value are apparent in a comparison of the blood pressure responses under ether and spinal anesthesia, in the group undergoing gastric resection for cancer (Table II). Under spinal anesthesia, unlike the circumstances when ether is used, even at the end of the first hour the circulation shows definite impairment; the peripheral resistance has been unable to compensate adequately; the cardiac output is unable to correct for this—not seriously so, but appreciably. It should be emphasized that this trend is not easily apparent from the examination of individual records. There is much more fluctuation of blood pressure and pulse rate during the course of operation in the course of a few minutes under spinal than is true under general anesthesia. This finding only becomes apparent when a considerable number of records are studied consecutively at one time. This fluctuation undoubtedly indicates strain on the circulatory system.

The changes encountered here in these average data are deceptively small; they show trends, not what may happen in an individual case. All of this information might be put down as so much academic straining over inconsequentials if it did not lead to the increasingly widely recognized observation that patients acutely subjected to trauma and to blood loss do in fact withstand spinal anesthesia less well than they do general anesthesia. The majority of reports from the European battlefields of this war as well as many reports from the previous war concur in this. Unhappily it is also roundly borne out by information now coming in from our own battle zones. *Spinal anesthesia is a poor procedure to use in the seriously wounded or the seriously impaired individual civil practice.*

In the group operated upon under local splanchnic block anesthesia the circulatory results at the end of the first hour are comparable to spinal, as might be expected. Interestingly enough, when sufficient time has elapsed for the splanchnic block to have waned, the blood pressure shows an upward trend. (Splanchnic block was frequently supplemented by light epival or subval or penthal sodium or other anesthesia.)

The patients operated upon under local anesthesia were obviously older, poorer risk patients. It is not fair to compare these data with the ether group. The inability of the circulatory system

of the impaired individuals of this last group to maintain original levels is plain. It was to be expected that this would be the case.

#### THE TECHNIQUE OF ANESTHESIA FOR TRANS- PLEURAL GASTRIC SURGERY

At the present time the anesthetist for thoracic surgery needs no more equipment than he does for a well conducted cholecystectomy. With one or two notable exceptions, the evolution from which present practices have grown has consisted not in acquiring new apparatuses but in discarding old ones. At the present time our technique has been reduced to what seems to require a bare minimum of equipment. Consideration of this may make the technique of anesthesia for transpleural surgery appear simple and it is simple although consideration of equipment alone may make it appear deceptively so. I wish neither to exaggerate its complexity nor to understate it. A primary aim of the work here has been to determine the essentials of a satisfactory technique, to show that a simple technique carried out with the equipment found in or easily obtainable by all reasonably well equipped hospitals, equipment familiar to well trained anesthetists, is adequate for this group of cases, provided certain cautions are unflinchingly observed.

In the transpleural approach to the upper abdominal viscera, the anesthetist can make a considerable contribution, for the anesthetist experienced in providing anesthesia for thoracic surgery can make it possible for the well trained general surgeon to operate in this field. The man who is experienced in gastric surgery can still do the gastric surgery by whatever route a physician indicates the choice to be. He is limited in the main by the experience and training of his anesthetist.

Reference has been made to the essentials of anesthesia technique for transpleural surgery. Elsewhere the principles (1) of anesthesia for this group of cases have been considered as well as the arguments (2) for and against certain current practices in this field. I shall not repeat these in detail here. From anesthesia for several broad major procedures through the open pleura we have concluded that the anesthesia for this group of cases should include: If the mortality is to be kept low the following:

Ether anesthesia briefly induced, its action oxidized in our choice. This is occasionally supplemented with procaine block of the vagus nerve and its pulmonary plexus as well as by frequent block of the phrenic nerve. Ether greatly depresses the activity of the vagus, a desirable condition

which we occasionally augment by rather large doses of atropine. Under ether, sensitivity of the respiratory center to carbon dioxide is preserved, a characteristic of great importance. The carbon dioxide blood level does not rise under ether as it does under certain anesthetic agents (4). Barbiturates, for example, in general anesthesia lessen and finally destroy the sensitivity of the respiratory center to carbon dioxide with sometimes fatal results, experimentally at least, but under circumstances very like those encountered in many clinical deaths.

Intratracheal intubation is essential, for it is only with an intratracheal tube in place that an open airway can be assured at all times. In our opinion it is unnecessary and unwise to use an inflatable cuff on these tubes. An intratracheal tube once in place eliminates the necessity for more or less frequent manipulation of the patient's head and jaws in an effort to improve the airway. Meddling here necessitates a deeper level of anesthesia than is the case if an intratracheal tube is in place and the airway left undisturbed. Reflexes from such a foreign body in the airway quickly fatigue and disappear. Thus, during wound closure the patient whose respiratory exchange will be excellent through the tube can be allowed to get very light, so that he has nearly recovered from the influence of the anesthetic at the end of the operation. The presence of the intratracheal tube also makes it possible to combat another possible hazard of the transpleural approach—the sudden, acute pulmonary edema which may develop if one lung long remains collapsed. If the transpleural approach to the stomach is to be of wide usefulness in the surgery of malignant disease, it should be possible to employ it in the aged. Elderly patients in this group may be prone to develop gross pulmonary edema if one lung is allowed to remain acutely collapsed. In no patient should the lung be allowed to remain collapsed for more than 30 minutes or so at a time. Only further experience with the aged group can tell us how often this accident will occur. In the meantime, facilities should be at hand to cope with it. An intratracheal tube is an indispensable aid in handling such a situation. Facilities for rapid bronchial aspiration, as well as positive pressure anesthesia when necessary, are important. A closed gas machine with carbon dioxide absorption and a tight face mask complete the list of essentials.

All parts of the technique referred to are essential if the major hazards of this type of anesthesia are to be overcome, namely, low blood oxygen, high blood carbon dioxide, obstructing

secretions, troublesome reflexes, including cough. Adequate provision for combatting these hazards must be made, we believe, if the transpleural approach is to be used successfully in gastric surgery.

The proper conduct of these cases requires that the rôle of the anesthetist be broadened. The anesthetist must take the responsibility for protecting the patient from needless strain. He warns against unnecessary heat loss in a too cold operating room, he minimizes harmful vagal reflexes by requesting that the vagus nerve or its branches be blocked with local anesthesia when cardiac and respiratory variations indicate the need, or he diminishes vagal activity by administering atropine, he watches for prodromal signs of shock and when necessary warns the surgeon of their development, he directs the administration of blood or blood substitutes, he guards against oxygen shortage or carbon dioxide excess.

#### CIVIL EXPERIENCE APPLICABLE TO ANESTHESIA FOR THE SURGICAL TREATMENT OF MAJOR WAR INJURIES OF THE THORAX

In the decade just passed it has been possible to distinguish between the dispensable and the indispensable anesthesia practices common in thoracic surgery. Great simplification has been possible in these. The excellence of ether anesthesia and the irreducible minimum of equipment necessary has been emphasized in this article and in the papers referred to in the discussion of the principles and procedures concerned.

The importance of the demonstration that simple procedures in this field are at least as effective as the many more complicated ones so often recommended becomes evident when it is recalled that an examination of battlefield dead of the last World War has shown that one-third died of chest injuries. Unquestionably many of these could have been saved by proper treatment. In the past the number of military deaths due to chest injuries has depended in large part upon the delay and distance to be overcome before these wounded can be transported to a hospital for definitive treatment.

We know that in the field of thoracic surgery more than in any other surgical field prompt treatment must be brought to the wounded patient rather than the other way around, if the patient is to be saved. The increased effectiveness and simplification of modern supportive measures and the simplification of anesthesia procedures go far to make thoracic surgery possible in combat zones. It is also apparent now that if the chest be open many abdominal procedures can be carried out through this same incision without unduly jeop-

ardizing the patient. This fact may be of use in military surgery.

The simplification of anesthesia principles and procedures important in thoracic surgery makes possible the rapid training to the point of adequacy of those who have had no special anesthesia experience in this field. *It is easier to train an anesthetist to the degree where he can make it possible for a well trained general surgeon to cope adequately with battlefield problems of thoracic surgery than it is to train a specialist in thoracic surgery.* However able the specialist may be he will be sadly handicapped if he must contend with poor anesthesia. However able the anesthetist may be he will seriously handicap his entire team if he insists upon elaborate equipment or procedures (3) already shown to be unnecessary in civil practice and certainly unnecessary in mobile battlefield surgery.

The anesthetist who is familiar with the problems of anesthesia for thoracic surgery can make it possible for the thoracic surgeon to proceed with deliberation in exploring thoracic wounds of warfare. It is the anesthetist who makes it possible for the surgeon to exercise the deliberation necessary for the proper control of hemorrhage, proper debridement of the wound, and to determine carefully what shall be done at once and what postponed. It is the anesthetist who makes it possible for the surgeon with only a general surgical training to work with success in this field.

#### SUMMARY

1. In a series of gastric resections for carcinoma, the tolerance of patients for the traditional transabdominal wall approach under ether is compared with their tolerance for the transpleural approach under ether, as far as surgical "fatigue" is concerned. It is observed that those in the trans-

pleural group tolerate the operative procedure at least as well and perhaps better than those in the other group. Thus when the transpleural route is indicated for anatomical reasons and when the operating team is experienced, it appears that the poor risk patient does not necessarily rule out the high approach.

Reasons for the patients' excellent tolerance for the transpleural approach to the stomach are found in the fact that in transpleural gastric surgery a far lighter level of anesthesia is possible than is true in the case of the transabdominal wall approach. In the former case the only relaxation needed is that of the diaphragm, obtained by block of the phrenic nerve under direct vision. Furthermore, in the transpleural approach to the stomach disturbance of the other abdominal viscera, well known to cause harmful circulatory effects, can largely be avoided.

2. When the gastric surgery is carried out through the anterior abdominal wall, evidence is presented that the circulatory system tolerates ether anesthesia better than spinal or splanchnic block anesthesia.

3. The indispensable anesthesia procedures used in performing transpleural gastric surgery are considered.

4. Lessons learned in civil practice that are applicable to anesthesia for surgical treatment of war injuries are considered.

#### REFERENCES

1. BRUCHER, HENRY A. *Acta med scand. Suppl. #* 933, pp. 46-57.  
*Idem. J. Thorac. Surg.* 940 10: 202-219.
2. *Idem. War Med.*, 942, 602-603.
3. BRUCHER, HENRY A., and MEYER, A. *J. Traumatol.* 1944.
4. CANNON, E. D. and S. *Brit. J. Surg.* 1944, 3: 897-97.

# A MODIFICATION OF THE CALLANDER AMPUTATION

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**T**HE Callander amputation has received wide recognition since its description (1935), and justly so, for it possesses certain definite advantages. As its originator has so strongly emphasized, the section goes through muscle tendons instead of muscle bellies, thus reducing the operative trauma and shock. Since the operative procedure is confined to the popliteal fossa, the spread of infection proximally along muscle planes is interfered with. The omission of deep sutures lessens the possibility of infection and favors primary union. The outline of the skin incisions, as shown by Callander, corresponds roughly to the distal extension of the collateral circulation when block is present in the popliteal artery. The absence of drainage material, though a detail, is also important in the avoidance of secondary infection and delayed healing. It is not within the scope of this paper to discuss the proper level of amputation, upper, middle, or lower thigh, knee (Callander), or proximal part of leg, under various pathological conditions. Suffice it to say that this depends, in my opinion, upon the type of pathological lesion—trauma, peripheral vascular disease, infection—and the condition of the circulation—main and collateral—in each individual case (see Grodinsky, 1938). However, since most leg amputations are done because of peripheral vascular disease, such as diabetes, senile arteriosclerosis, Buerger's disease, they are usually done high, at or above the knee, to insure healing of the stump.

Amputations through the middle or proximal thigh are accompanied by considerable postoperative shock due to cutting through muscle bellies and sometimes result in poor stumps for the use of artificial legs. The Gritti-Stokes operation was an earlier attempt to get high enough for good healing and still have a good stump for weight bearing. Its great fault lay in the uncertain and insecure union of the retained portion of the patella to the cut end of the femur. The Callander operation, by removing the patella and transecting the femur just above the articular surface, has obviated these difficulties while retaining the other advantages of the Gritti-Stokes procedure.

However, the Callander operation has, in my opinion, one serious fault, that of long skin flaps.

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It has long been recognized that short flaps, or no flaps at all, favor primary union in amputations for peripheral vascular disease. It is true that the collateral circulation, in case of occlusion of the popliteal artery in the popliteal fossa, is usually sufficient to maintain vitality in the skin and subcutaneous structures roughly corresponding to the proximal third of the leg. However, this is only true under conditions of rest and protection. When the trauma of operation, no matter how gently performed, is added to the picture, the outcome is often different. It has been my misfortune and that of others (e.g. Pearl, 1941) to have had several cases of sloughing or slowly healing flaps following the classical Callander operation. For that reason, I gradually modified the operation by progressively shortening the flaps, while retaining the other essential features of the original operation. The results by the technique thus gradually evolved have been, in my experience, far superior to those with the original operation as regards healing time and satisfactory stumps. The modified technique of Pearl (1941) is, in my opinion, inadequate because the skin flaps are still too long, the patellar bed is not retained to support the lower end of the femur, and the latter is transected higher than necessary.

## TECHNIQUE

**Incisions.** No tourniquet is used in any amputation done because of peripheral vascular disease for fear of further damaging diseased blood vessels. The skin preparation and draping are done in the usual manner. With the operator standing to the medial side of the leg to be amputated and with the knee slightly flexed, the skin incision (Fig. 1) for the anterior flap is started just distal to the patella and carried medially in a curved direction to a point about 1 inch proximal to the medial condyle of the femur. Then it is carried laterally in a similar manner to a point about 1 inch proximal to the lateral condyle of the femur. The posterior flap is made the same length as the anterior one, and the incision, starting in the popliteal fossa opposite the distal border of the patella, extends in both directions to meet the medial and lateral ends of the anterior incision already made. This is practically a circular incision with slight proximal extensions medially and laterally to facilitate the exposure and section of the deeper



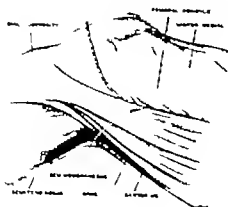


Fig. 2



Fig. 3



Fig. 4

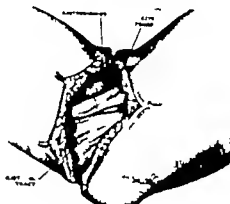


Fig. 5

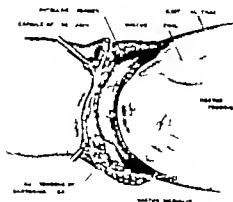


Fig. 6

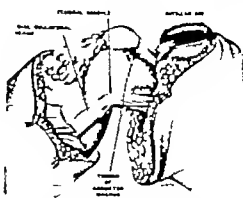


Fig. 7

Fig. 2. Medial aspect of right knee region, showing out line of skin incisions—medial in solid lines and lateral broken lines—in relation to bony prominences and muscles. Not short, equal flaps.

Fig. 3. Deep view medial side—tendons of medial muscles being elevated for section in line. In skin incision. Fig. 4. Deeper dissection from medial side showing method of detachment and doubly ligating popliteal vessels.

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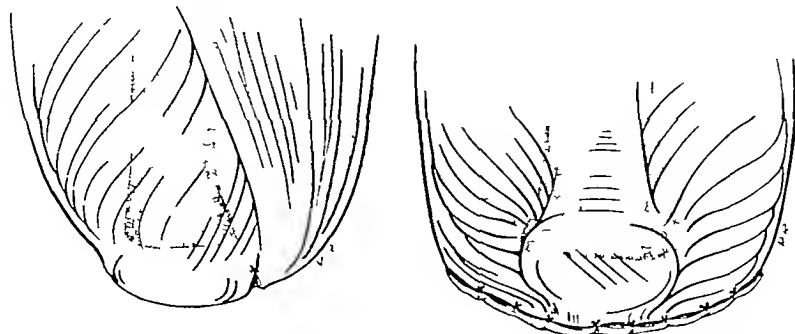


Fig 7 Diagrammatic transparency drawings of stump, medial and anterior views showing relation of the end of the femur to the overlying muscles and to the suture line. Note how the patellar fossa fits over the lower end of the femur.

structures. The medial extension should pass between the vastus medialis and sartorius muscles and the lateral extension between the iliotibial tract (the continuation of the tensor fascia lata) and biceps femoris muscle.

*Treatment of medial side and popliteal fossa*

With the leg rotated laterally, the skin incisions are deepened both anteriorly and posteriorly from their middle to their medial extremities, so as to expose the tendons of insertion of the sartorius, gracilis, semitendinosus, and semimembranosus muscles. Each of these is transected opposite the proximal border of the skin, the skin having retracted somewhat by this time (Fig 2). This exposes the popliteal space containing the main vessels and nerves. The popliteal artery and veins are easily delivered into view, doubly ligated with No. 2 chromic catgut and severed between ligatures (Fig 3). An additional ligature on the proximal side of the artery is usually desirable. The tibial and peroneal nerves are likewise delivered from the fossa, either together or separately, depending on the individual case. They are also doubly ligated with plain or chromic catgut,

injected between the ligatures with 1 to 2 cubic centimeters of 95 per cent alcohol, and then transected through this area, between the ligatures. As pointed out by Pearl (1941), this method of alcohol injection prevents proximal extension of the alcohol and undesired effects therefrom.

*Treatment of lateral side* By rotating the limb toward the operator, a good exposure of the lateral aspect may be obtained. The lateral halves of the anterior and posterior incisions are deepened to expose the iliotibial tract and the tendon of the biceps femoris muscle. These are transected opposite the proximal border of the skin incision in the same manner as the tendons of the medial side. The remaining soft—areolar—tissues in the popliteal fossa are likewise transected opposite the proximal border of the skin incision, thus completely freeing the posterior as well as the medial and lateral surfaces of the femur (Fig 4).

*Anterior dissection* With the limb in the original position, the anterior incision just distal to the patella is deepened so as to extend through the patellar tendon and its medial and lateral extensions and expose the knee joint (Fig 5). The patella is quickly cut from its bed without attempting to destroy the adjacent serous surface.

*Transection of femur and treatment of stump* The insertion of the adductor magnus is separated from the adductor tubercle and, after the soft tissues are protected by towels, the operator transects the femur just proximal to the adductor tubercle with ordinary or Gigli saw (Fig 6). The edges of the bone are smoothed off with a file or rasp and the bleeding points sealed with bone wax. The soft tissues of the stump are irrigated with warm saline solution to wash out all debris and bone dust, and the bleeding points are ligated with fine plain catgut. No deep sutures are placed but the skin flaps are loosely brought together by

preliminary to sectioning between ligatures. Note additional ligature on proximal side of popliteal artery. Insert shows method of delivering and doubly ligating sciatic nerve, before injecting with alcohol and sectioning between ligatures.

Fig 4 Lateral view of rotated right knee region, showing deepened skin incision with exposure of the iliotibial tract and the biceps femoris muscle. The site of section of the tendon of the latter on level with the skin incision is indicated by the broken line.

Fig 5 Anterior view of right knee region showing deepened skin incision, and site of section through patellar ligament and capsule of knee joint, broken line.

Fig 6 Deepest view of anteromedial aspect, showing sectioned muscle tendons, vessels and nerve, the patellar bed after removal of the patella, and the line of section of the femur just above the adductor tubercle.

widely spaced skin clips or dermal sutures, leaving sufficient spaces between clips or sutures for drainage (Fig. 7). Usually only three or four clips or sutures are needed on each side. After 48 to 72 hours, when most drainage has ceased, additional clips or sutures may be placed between the original ones for better coaptation. Ordinary dry dressings are applied, a good dressing being a 5 yard roll followed by flannel or gauze bandage. Ordinarily traction is unnecessary and the patient is returned to bed with the stump slightly flexed on pillows.

*After treatment.* In the absence of excessive fever or pain it is not necessary to re-examine the wound before 72 hours have elapsed. At that time, if the drainage has apparently ceased, the additional clips or sutures may be introduced and the stump dressed as before. In the absence of further temperature reaction or other untoward symptoms, the stump does not have to be examined again until the 8th day when alternate clips or sutures are removed. The remaining clips or sutures are removed between the

10th and 14th days at which time if healing is by primary or almost primary union the patient may be discharged from the hospital and treated thereafter at home or in the out-patient department.

#### RESULTS

Although the flaps are not as long as in the original Callander operation, they are of sufficient length to permit easy closure of the skin as described. As usual, the greater retraction of the hamstrings brings the scar posteriorly so that even with an end-bearing artificial limb, perfect scar results. As in the Callander operation, the patellar bed covers the end of the femur forming a satisfactory pad for the latter. A smooth conical stump results which facilitates the fitting of an artificial limb if one is to be worn.

#### REFERENCES

- CALLANDER, C. L. *J. Am. M. Ass.* 935, 5, 1774-753.
- GEORGE, M. *Am. J. Surg.* 935, 4, 339-345.
- PEARL, F. L. *Surg. Gyn. Obst.* 94, 71, 31-37.

# THE SHOCK CART

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**I**N THE study of surgical shock cases at the Presbyterian Hospital, New York, we have found that by assembling equipment on a cart the time for obtaining objective data has been shortened by taking the laboratory to the patient's bedside

For the past 5 years, certain simple tests have given us a clearer and less subjective approach to the question of what to do in acute emergencies, what fluids to select and above all when fluid therapy should be changed or stopped (4)

These tests supplement a careful history and physical examination They are

1 *Specific gravity of peripheral blood* (1, 2) It is here that changes first appear Hemoconcentration in the *capillaries* foretells of the approaching fall in blood pressure

2 *Hematocrit on venous blood* In shock, excluding that due to hemorrhage, a decreasing hematocrit indicates that blood volume is being restored On the other hand, should repeated hematocrits or repeated determinations of specific gravity of capillary blood reveal that hemoconcentration is occurring in spite of therapy the warning is clear, either, the lesion is overwhelming, or, the supportive therapy is insufficient or wrong and should be changed

3 *The specific gravity of plasma* This is done on the supernatant fluid in the hematocrit tube

4 *Total plasma protein* From tables, the specific gravity of the plasma is readily translated into total protein concentration according to the formulas of Weech, Reeves, and Goettsch, or Moore and Van Slyke

Every hematocrit should be checked by total protein determinations We recommend that a base line be secured on admission, or as early as feasible, and that repeated determinations be instituted Single values are of little importance Trends in hemoconcentration or hemodilution are significant

*Elapsed time for tests* With a little practice, the specific gravity of plasma or capillary blood can be ascertained within 2 or 3 minutes We usually spin the hematocrit for 1 hour to secure ultimate packing In emergencies, the centrifuge can be stopped at the end of 15 minutes This

reading will be within 5 to 10 per cent of the true value

In addition to diagnostic procedures, therapeutic remedies such as liquid or dried plasma, isotonic or hypertonic (5%) saline, whole blood, and adrenal cortical extract can be easily transported on this cart If there are a number of casualties, the cart affords space for carrying sufficient blood and other remedial measures

*Field transportation* A carrying case for the falling drop apparatus, hematocrit tubes, solutions, etc., has been used in trips about the country and in journeys abroad This case has been tested out in all kinds of travel from the airplane

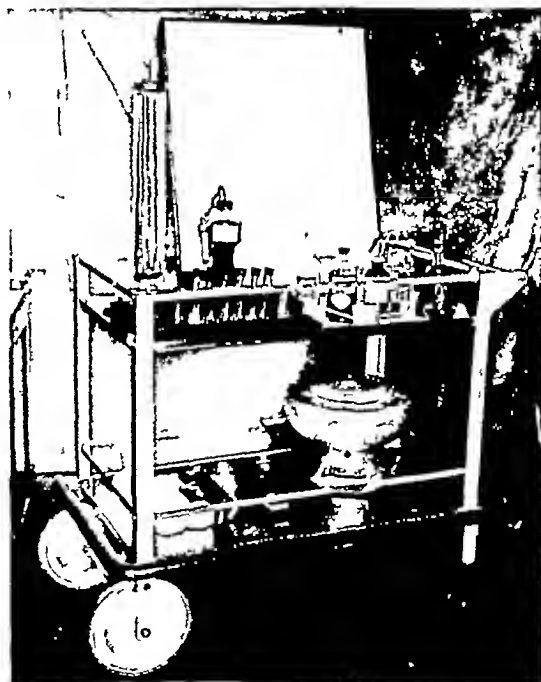


Fig 1 The shock cart The following items are carried on the cart alcohol, tourniquet, sponge jar, sponge forceps, sterile sponges, lancet, kidney basin, hematocrit tubes with heparin, test tube rack for hematocrit tubes, sterile, dry 20 c c syringes, ammonia, water, alcohol and ether for cleaning pipettes falling drop apparatus, pipettes, pipette holder, stopwatch and stand, alignment chart, specific gravity standard solutions, extra xylene-bromobenzene mixtures, centrifuge, pencil, paper, flashlight Cut down set for cannulation of veins

From the Surgical Pathology Laboratory of the College of Physicians and Surgeons Columbia University, and the Department of Surgery the Presbyterian Hospital New York New York

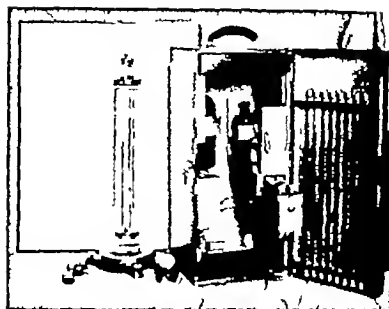


Fig. Carrying case.

to an o. cart. The use of a hand centrifuge obviates the necessity of electrical power.

*Distribution of apparatus.* In 493 hospitals and laboratories these tests have been adopted.

Finally in the training of young surgeons for the armed forces it should be the duty of those who remain behind in the teaching centers to inculcate the necessity of the present quantitative approach to shock and to have these students follow such cases with these exact measures.

## REFERENCES

- BARRETT, H. G. and HARRISON, W. F. *J. Biol. Chem.*, 926 to 935-420.
- Idem. *J. Am. M. Ass.* 927 85 9-43.
2. MOORE, A. S. and A. SUTER, D. D. *J. Clin. Invest.* 930, 8 337-355.
3. " " " " Shock, Blood Studies as Cause in Therapy. Philadelphia, Moore, Lander, J. B. Lippincott Co. 94.
4. WELCH, A. A. REIDY, E. B. and CARTER, I. *J. Biol. Chem.* 935, 3 67-74.

# AN AMBULATORY METHOD OF TREATMENT FOR INTERTROCHANTERIC FRACTURES OF THE FEMUR

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ONE of the most frequent accidents of later life is fracture of the hip. Until the development by Smith-Petersen of the three flanged nail, at a time when isoelectric metals were available, no outstanding advance had been made in their treatment. While this nail was successful in the treatment of intercapsular fractures it did not solve the problem of fractures in the intertrochanteric area, especially when severe comminution was present.

The following is a description of a method of fixation that is applicable in any type of intertrochanteric fracture. It does not confine the patient nor require an incision, it immobilizes no joints and permits early crutch ambulation. No other method described in the literature combines its simplicity, universal application, or its advantages. Fifty-four patients have been treated by this method, 22 of which by other operators.

There is wide variation in the position of the fracture lines and in the degree of impaction and comminution in intertrochanteric fractures of the femur. The fracturing force and muscle spasm tend to pull both fragments upward, creating a *cova vara*. The lower fragment, if not impacted, tends to fall backward and into external rotation, due to the weight of the extremity. The lesser trochanter may be detached, especially in severe comminution, or may remain intact with the proximal fragment, in which case the proximal fragment tends to be displaced upward along the course of the iliopsoas.

Regardless of the method of treatment, accurate reduction and firm fixation of the fragments are necessary in order to obtain early union. Reduction is usually made possible through longitudinal and lateral traction, while the distal fragment is lifted, abducted, and internally rotated. The usual attempts at immobilization are made through the medium of a body cast, with or without traction, or such forms of traction as are used with the Thomas or Hodgen splints, or traction on the principle of the Roger Anderson well leg method. Open operation with fixation by means of a combination of plates, nails, or screws may be used in the less comminuted types.

The use of a body cast, or any method of traction, requires a long period of close confinement.

It may be necessary to maintain the abduction and traction treatment for a period of 6 months or more to secure solid union, because if fixation is not complete, union may be delayed. If the limb is freed before union is firm, muscle pull acting on the soft callus results in a *cova vara* and infrequently in nonunion. The use of a plate with a nail or screw is not a simple procedure. The equipment is expensive and its use is of limited application because it is not suitable for many severely comminuted fractures.

In treatment by means of a body cast or a method of traction, nursing care is often a serious problem because of the distress of confinement, discomfort of incomplete fixation, pain of pressure sores, hypostatic pneumonia, or because of the physical and mental deterioration that follows long immobilization in elderly people. Even after the fracture has healed invalidism may persist due to stiff knees and hips or to the physical weakness that follows long inactivity.

In this method fixation of the fragments is secured through the closed insertion of four pins. Two pass within the neck into the head of the femur and are firmly united with two passing at a converging angle through the upper end of the distal fragment. This unit creates a solid bridge across the fractured area between the head and the upper end of the distal fragment of the femur and accomplishes complete fixation in any type of intertrochanteric fracture. The patient is not confined, may move about in bed immediately following the operation, and be up in a chair, the more active patient be on crutches, in a few days. All joints are kept mobile, so that the patient's strength is better maintained and his mental attitude kept more cheerful. As a result, pressure sores, pneumonia, and degenerative changes are less frequent, which fact greatly simplifies nursing care, shortens hospitalization and duration of disability following healing.

In the care of an intertrochanteric fracture, treatment of shock is undertaken immediately. This treatment will usually include traction immobilization of the extremity. Early reduction and fixation of the fragments are desirable, for they will minimize shock and lessen the incidence of physical and mental exhaustion.

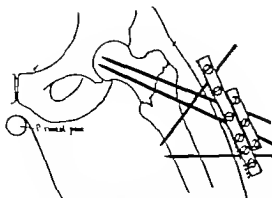


Fig. 1. Anteroposterior view of the fixation in place. The dotted line represents the initial plaster first applied. The long clamp is on the distal pin, and the short one on the proximal one. This unit is later incorporated in plaster cast to the thigh as described.

For reduction, the anesthetic needed will vary with the patient. The routine use of  $1\frac{1}{2}$  grains of nembutal with  $\frac{1}{2}$  grain of morphine and  $\frac{1}{100}$  grain of scopolamine an hour before surgery will suffice for reduction in a number of patients, while the addition of 20 to 30 cubic centimeters of 1 per cent novocain injected into the fracture site will permit reduction in the majority. However, the most satisfactory state of anesthesia is obtained by the additional use of pentothal, very little being required for narcosis.

After reduction the legs are immobilized in traction, with the injured member parallel to the floor abducted, rotated, and with traction sufficient to maintain the reduction. The uninjured leg is extended but permitted to drop about 12 inches lower at the heel than its fellow in order to facilitate the taking of lateral roentgenograms. Anteroposterior and lateral ray films are always taken to check the reduction and placement of pins. Unless they are properly taken the results may be most misleading and time consuming. The ray must be centered on the neck in both the vertical and horizontal planes, and repeat ray films must be taken from the same viewpoint. If not properly centered distortion may cause a poorly placed pin to appear well placed, while films taken from various viewpoints have little value for comparison. The center of the proximal portion of the head will be at a point proximately  $\frac{1}{2}$  inch below the midpoint of a line joining the anterosuperior spine and the lower border of the pubis. A perpendicular line intersecting this point will approximate the center of the neck, and to obtain the anteroposterior view the ray should be centered 1 inch distal along this

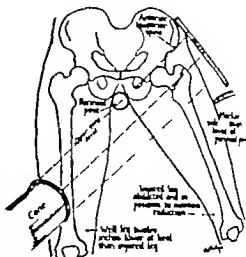


Fig. 2. View from above when lateral ray film is taken. The marker shown is used as guide for the position of the first pin when the anteroposterior view is taken.

line. The lateral view is obtained by placing the tube at the side of the well leg with the cone directed over the leg. The rays should be parallel to and include the line joining the anterosuperior spine and the peroneal point, the plate being held well in the flank at right angles to the cone. This technique will permit repeat ray films from the same viewpoints, the alignments being each and quickly made without movement of either extremity. As most of the older fracture tables, such as the Howley, have an iron pelvic rest and peroneal point it is necessary to replace them with wooden units in order to use this technique; otherwise the head will be undefined in either view being obscured by the metal parts.

Reduction being satisfactory careful surgical preparation is made of the thigh before insertion of the pins. First to be inserted are those which are to pass through the neck into the head of the femur to control the proximal fragment. These pins are 6 inches or more in length, depending upon the depth of the soft tissues,  $\frac{1}{8}$  inch in diameter sufficiently heavy to support the weight of the patient in case of weight bearing, and are easily inserted by means of a T handle. The correct placement of the first of these upon the initial attempt is the most difficult part of the procedure. As a guide for the selection of the point of insertion a marker is placed on the lateral surface of the thigh at the level of the peroneal point when the anteroposterior view is being taken. The film will indicate point of relation; the marker at which the pin must enter the soft tissues is



Fig 3 Case 2 a, February 18, 1941 fracture in an 84 year old female b, February 20, 1941, anteroposterior view of reduction and fixation pins in place c, February 20, 1941, lateral view of reduction and pins in proximal

fragment d March 12 1941 view of fixation Patient had been on crutches 1 week e October 27, 1941, final result Excellent functional result The pins were removed May 6, 1941

order to enter and parallel the long axis of the neck of the femur in the horizontal body plane. The lateral view will indicate the amount of inclination needed to parallel the long axis of the neck in the vertical plane. After the point and angles of insertion have been determined, the pin is felt to pass easily through the soft tissues and strike the relatively dense cortical surface. When it is through the cortex, it passes readily through the neck and strikes the compact bone of the head into which it should enter about 1 inch. X-ray films are then taken to check the position and the second pin is inserted, with the position of the first used as a guide. If the first was not properly placed it may now be adjusted

Control of the distal fragment is secured by two additional pins in its proximal end. These are 5 inches or more in length and are  $\frac{1}{32}$  inch in diameter. They are inserted at an angle to one another so that they bear the same relation as two sides of a triangle to one another. Each must pass through both cortical surfaces of the femur and preferably in the same horizontal body plane as those in the proximal fragment. These two pins utilize the principle of the Roger Anderson half pin unit, a number of which were used in this series to secure the distal fragment.

Sterile dry dressings are placed over the pins, and a layer of sheet wadding is applied about the thigh, followed by a number of turns of plaster



which embrace the pins and firmly and smoothly press the soft tissues along the pins toward the shaft. To secure complete fixation of the fragments the four pins must be firmly united with one another and to unite them more firmly than is possible with plaster alone two flat pieces of metal bar of the shape of tongue blades, which have been drilled and tapped so that they may be tightened together by means of a number of screws or bolts, are used as a clamp over the pins. A clamp is placed about each set of pins, made snug against the plaster that has been applied, and solidly tightened on the pins. The clamps and pins are united by plaster and incorporated in a light cast to the thigh, its extent being such that free motion of the hip and knee is possible.

Immediately after the cast has hardened the thigh and knee should be put through a full range of motion. This will separate the fascia and muscles along the pin tracts and lessen the discomfort of early active motion. The day following the operation the patient may sit up in bed and, as his general condition improves, be up in a wheelchair and on crutches. In the mean time immediate passive motion is made gently daily in the hip and knee and active motion as soon as is encouraged.

The pins are left in until union is solid, as disclosed by x-ray film which is usually within 6 to 10 weeks.

In the application of this method certain factors will contribute to its success and to the comfort of the patient. Special effort should be made to insert the pins so that the soft structures are without tension, for when tension is present there will be discomfort and pressure necrosis with exudate. The presence of exudate or bleeding about the

pins will result in moist dressings and is an invitation to infection. Early active motion must be insistently developed and this is facilitated through early gentle passive motion and use of the wheelchair with the leg in flexion.

The only points of solid fixation of the pins in the proximal fragment are those portions which are in the head. For this reason they should be inserted well into the head and below the upper margin especially in case of long standing trochanteric disturbance, because the constant muscle pull and occasional weight bearing may cause them to cut through the softened head and neck and result in loss of fixation.

In conclusion a method of multiple pin fixation is presented for all types of intertrochanteric fractures of the femur. It is simple in application, requires no fixation, immobilizes no joint, and permits early crutch ambulation.

#### REFERENCES

- ANDERSON, ROGER. *Surg. Gyn. Obst.* 1932, 54, 207.
- Idem. *South Surgeon*, 1930, 8, 50-72.
- CARRSBERG, MUEL R. V. *Surg. Gyn. Obst.* 1941, 71, 772-777.
- CLARK, E. R. and MORSEMAN, GEORGE M. *West. J. Bone Surg.* 1940, 3-136.
- FOW, THOMPSON A. and ARTHUR, GEORGE L. *J. Bone Surg.* 1941, 3, 352-360.
- JONES, CARL P. *California West. M. J.* 1931, 34, 7-16.
- KIPP, J. *Western Surgery*, 1930, 6, 1-3.
- LEITCH, S. WILSON M. and BARON, THOMAS P. *J. Missouri M. Assn.* 1940, 37, 254-257.
- LEITCH, S. WILSON K. *J. Missouri State Hosp. N. Y.* 1941, 2, 459-466.
- MORSEMAN, GEORGE M. *South M. J.* 1941, 34, 57-61.
- MORSEMAN, GEORGE M. *J. Tennessee M. Assn.* 1941, 3-6.
- SILVERMAN, E. and CLARK, E. R. *J. N. Y. Surg.* 1940, 47, 43-44.

# ARTHROPLASTY OF THE HIP FOR OSTEOARTHRITIS UTILIZING FOREIGN-BODY CUPS OF PLASTIC

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THIS presentation will deal with two subjects arthroplasty utilizing foreign substances of nonanimal origin and end-results of these and other methods in ameliorating pain and disability in osteoarthritis of the hip. Péan and Chlumsky were the first to utilize foreign materials in arthroplasty, the former in human joints, while the latter experimented with an array of metal plates and films of celluloid, rubber, and collodion. Sir Robert Jones, utilized a strip of gold foil to cover the reconstructed head of the femur. He reported 21 years later that motion was still present in the reconstructed joint. Pupovac reported the temporary success of a magnesium plate in an arthroplasty. Rehn, however, appears to be the first to grasp the principles of a cup arthroplasty when he inserted into the hip a previously molded cap-like appliance of steel, spiked upon the acetabular side. This appliance was removed 8 weeks after the first operation. At this second stage he interposed an autogenous graft of fat and fascia. Smith-Peterson (45) has utilized cups of various materials glass, viscaloid, pyrex glass, bakelite, prior to his adoption of vitalium cups. While he appears not to have further explored the possibilities of nonmetallic cups, bakelite was apparently satisfactory in 1 case, as he wrote that "the mold is still in place (2 years after the operation) and the patient is doing well." The disease for which this operation was performed and the ranges of preoperative and postoperative motion were not given. Payr and the MacAuslands have summarized the subject of arthroplasty in their books.

The successful application of the cup principle to arthroplasty of the hip came with the utilization in surgery of the newer metal alloys, especially vitalium. Hopkins and Zuck reported the first use of a vitalium cup for hip joint arthroplasty in a patient suffering from osteoarthritis of this joint following trauma. Smith-Peterson (45) reported upon the use of a flanged vitalium

cup, and at about the same time Venable and Stuck reported upon a mold of this same metal which they affixed to the femoral head. Smith-Peterson's cup is allowed to remain more or less free, being attached neither to the femoral head nor to the acetabulum, while its small everted rim anchors it loosely in the acetabulum. Its shape would lead one to believe that the majority of motion is secured between the mold and the femoral head. Venable and Stuck fix their cup to the femoral head and neck by a vitalium screw. Another technical variation has been introduced by Preston who uses a flanged cup fixed to the contour of the acetabular margin by an irregular rim. Further discussion of the desirable shape for the hip cup will appear in a later section of this paper.

In recent years many individual reports of arthroplastic operations upon the hip have appeared in the surgical literature. These have been quoted and summarized elsewhere (MacAusland and MacAusland, Murphy, and Payr) and, in the main, are of historical interest only, contributing little to modern conceptions of arthroplasty. Reports of end-results, following hip arthroplasty for osteoarthritis in which autogenous fascia lata was used, are of interest in establishing a standard for comparison to the cases reported herein. Campbell (7) stated that he had obtained 60 per cent good results in his cases, but a later detailed analysis of his cases, even though not classified according to the present accepted nomenclature for arthritis, leaves the impression that the percentage of satisfactory results was not as great in persons suffering from "chronic arthritis." Hallock (11) reported on the end-results of 70 arthroplasties and reconstruction operations upon the hip joint, of which 24 were cases of osteoarthritis of this joint. In this group of cases pain was considerably alleviated but average motion was lost. This author indicated that the results were "much better" when proper selection of cases and newer operative principles obtained. Fuiks reported the end-results from single layer autogenous fascia lata arthroplasties in 60 patients operated upon in Steindler's clinic. Of these cases, 15 were instances of osteoarthritis of the hip. The results were de-

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Read in part at a meeting, of the Chicago Orthopedic Society, March 14, 1941, and at the Philadelphia Orthopedic Society, December 10, 1942.

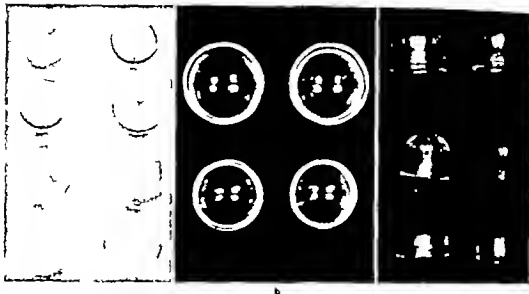


Fig. Types of methacrylate cups for hip-joint arthroplasty. a, An assembly of plain cups of approved size. The three smallest sizes are for the majority of patients.

b, Cups having heavy stainless steel liners in the rim. These cups permit the observer to rock (gray studies). c, Long and short cups. The long cups inhibit motion and are not preferred.

scribed as good, in 46 per cent and fair in 40 per cent, a total of 86 per cent. The significance of a good result was one in which there was at least 45 degrees of flexion and no pain. The results were classified as fair when there was less than 45 degrees but more than 20 degrees of motion, and the patient had little or no pain and was personally well satisfied with the result, either because of decreased pain, increased motion, or better position of the limb. In our experience the final results vary depending upon the original motion prior to operation upon the osteoarthritic hip. This factor was not considered by any of the previous authors in reporting end-results.

While titanium is desirable for this purpose because it is electrically inert in the tissues, it possesses, like any metal the unfavorable property of being radio-opaque. Changes in the femoral head stump, which are known to occur with frequency following membrane arthroplasty, cannot be visualized through this metallic foreign body. Aseptic necrosis of the femoral head probably occurs, in a certain percentage of cases, following cup arthroplasty. Indeed, Ferguson states that it is not possible to remove more than one-third of the circumference of the femoral head (arthroplastic procedure) because absorption of the remaining portion will often occur (due to aseptic necrosis and pressure destruction). Some of the indifferent results that

have occurred following the use of titanium cups may be due to proliferation of new bone about the acetabular rim or from the femoral neck around the cup margins, or to septic and pressure necrosis of the remodeled femoral stump (2, 11, 36, 40). Pain, present in a certain percentage of cases in which metal cups are used, may possibly be due to the hardness of the weight-bearing surface.

In searching for a material (16, 17) that would possess the property of radiotransparency and still be well tolerated by the tissues, the author's attention was directed to the group of plastic materials which have come into recent general use in industry. From a consideration of physical properties the methacrylate resins (Lucite and Plexiglas) and the polystyrenes were selected. The methacrylate plastics<sup>1</sup> only were used in the cases reported in this paper. These substances are polymers of methyl methacrylate. When cast in rods, sheets, or blocks, the material is crystal clear, light in weight (specific gravity 1.18) and slightly flexible, but is also durable and strong as evidenced by the following physical constant: tensile strength, 9,000 to 12,000 pounds per square inch; flexural strength, 12,000 to

<sup>1</sup>For more description of "Lucite," see DuPont Plastic on an industrial basis, L. F. DuPont, in *Chemistry and Commerce of Plastics and Films* (London, 1947). In another methacrylate plastic, "Plexiglas," cups utilized in this report have been manufactured in and long known and kept methacrylate plastic (Lucite, Plexiglas, etc.).



a



b



c

Fig 2 Early changes of osteoarthritis in the hip a, Hips of a young man of 33 years Advanced changes in one hip and early changes in the contralateral hip The latter, although asymptomatic and having normal joint space, demonstrates early osteophyte formation on the anterior and superior neck and the early inferior adductor atrophy and osteophyte formation b, A stage slightly

more advanced In addition to the early stages noted in a, supra acetabular and femoral head sclerosis is present c, Another type of early change consisting of a wedge-shaped osseous infarct, which has undergone retransformation into living bone at its base Pain, however, without limitation of motion, was present in the case of this patient

14,000 pounds per square inch, impact resistance, 0.1 to 0.3 foot-pound, hardness (Brinell) 500 kilograms on 10 millimeter ball, 17-20 It may be cut, turned, sawed, carved, drilled, polished, shaped, formed, and swaged It has a negligible water absorption since less than 0.5 per cent by weight is absorbed upon immersion for 7 days, and is resistant to sun and ordinary atmospheric exposure Solid methacrylate is not affected by alkalis, oils, dilute acids, solutions of mineral salts, and dilute alcohol

Cast methacrylate will not soften until 190 to 240 degrees F has been reached, while moldings will withstand 140 to 190 degrees F, depending upon whether prepared from "soft" or "hard" powder The polystyrene plastics are similarly resistant Both these substances retain only traces of irritating solvents called "plasticizers" in industry, while the phenolic plastics retain appreciable amounts of these materials For our purposes, the methacrylate hemispheric cups were sterilized by prolonged (1 hour) immersion in a 0.2 per cent solution of mercuric oxycyanide, followed by rinsing in sterile distilled water Mercuric chloride solution (0.1 per cent) has also been used Figure 1 shows an assembly of plastic cups The two small cups were found to fit the trimmed femoral heads in the majority of cases The walls of the cups were  $3/32$  and  $3/16$  inches thick and the cup itself was molded into hemispheric shape The radius of depth of these cups was less than their internal cross-sectional radius ( $3/4$  and  $7/8$  inches) The two larger cups, used infrequently, had an internal cross-sectional radius of  $15/16$  and 1 inch, respectively

#### ANATOMY OF THE HIP

The conventional conception of the normal hip as a "ball and socket joint" is inadequate The normal femoral head represents about two-thirds of a true sphere, the circular cross-sectional base of which becomes continuous with a near cylindrical femoral neck, which structure bulges on either end The center of curvature of the portion of the sphere that is the femoral head does not lie in the plane of junction of head and femoral neck, but in a plane about one-third of the distance between the plane of junction of head and neck and a tangential peripheral plane that passes through the central fovea of the head The aim of the cup arthroplasty, to be described later, is to decrease the enlarged volume of the irregular osteoarthritic femoral head, to restore a presenting true spherical surface, and to cap it with the hollow plastic hemisphere A true sphere is the only presenting surface that will not further restrict motion Cup-like molds, whose radius of depth exceeds the maximal cross-section radius (Fig 1c), further restrict motion by impingement of the excess length of the cup margins upon the femoral neck and acetabular margins This fact has been verified at operation upon many occasions

The acetabular margins are higher superiorly and posteriorly and are defective in an inferior (acetabular) notch, covered in the living by transverse ligaments The acetabular cavity presents laterally and inferiorly The interior of the acetabulum is far from being a true "socket" or "cup" The superior and posterior roof contains a slightly elevated condensation of osseous articu-



Fig. 3. Moderately advanced changes of osteoarthritis of the hip. a. Shows narrowing of joint space, osteophyte production on both femoral head and acetabulum and sclerosis (then the head). These changes are secondary to pyogenic arthritis of the hip many years before. b. Changes within the head and marked spur-like osteophyte formation in the adductor region of both acetabulum and femoral head. Supra-acetabular sclerosis is more marked than in, a.



Fig. 4. Advanced changes of osteoarthritis of the hip. a. One hip of a case secondary to bilaterally congenital inadequate acetabula, (distinct dislocation). Cysts are seen within the head, large adductive femoral head osteophytes and sclerosis and new bone formation in the superior portion of the joint. b. Single hip from similar bilateral case (primary). This demonstrates, in addition to other changes, degenerative ramifying adductive osteophytes.

lar cortex not exceeding one third to one half of the total internal surface of the acetabulum. This prominent and raised osseous portion represents the weight bearing zone of the acetabulum and is visualized in the conventional anteroposterior roentgenograms as the acetabular roof. The articular cartilage fills in the remainder of the acetabulum with the exception of the fovea. In the living normal hip the presenting articular surface is smooth, the cartilage covering the weight bearing osseous surfaces being thinner than elsewhere. The variations of the structures that are encountered in operative surgery upon the osteoarthritic hip will be described in the following section.

The normal adult femoral head varies in diameter, being largest in the male. The few direct measurements that have been made of operation indicate the normal diameter to be between 2 1/8 and 2 inches. The largest male femoral heads may even approximate 2 3/4 inches, while the smallest female heads may have a diameter approximating the first mentioned figure, some are as small as 1 3/4 inches. Even though considerable variation has been encountered in the femoral head, the transverse diameter of the femoral neck at the midpoint between its junction with the head and the cervicotrochanteric junction is almost constant at 7/8 inch with maximal variations of 1/16 inch. A fair approximation of the osseous femoral head may be obtained from roentgeno-

grams, when the distortion factor of approximately 0.9 at a 3 foot 1.5 inch distance and an 8 centimeter object to film distance are borne in mind.

#### GROSS AND MICROSCOPIC ALTERATION OF THE OSTEOARTHRITIC FEMORAL HEAD

The following description is based upon the study of roentgenograms of 91 osteoarthritic hips from the files of the Guthrie Clinic and the Robert Packard Hospital and from the direct observations of approximately 60 osteoarthritic hips at operation, including those reported heretofore. The histories presented by the patients are reviewed in the succeeding section dealing with etiology and pathogenesis of osteoarthritis of the hip and in the appended case reports.

The changes to be seen in roentgenograms of the early osteoarthritic hip (Figs. 2a and 2b) include marginal osteophytes at the head-neck junction, flattening of the lateral acetabular margin, widening of the head by growth of the adductor part of the head, as seen in the anteroposterior film, and sclerosis within the head and above the acetabular articular bony cortex (supra-acetabular sclerosis). At this time the superior joint space (anterior space) may be normal or slightly diminished (Fig. 3). As further changes take place spotty sclerosis appears in the head (Figs. 2b, 3a and 3b) (denoting osseous infarction or endosteal proliferation). Marginal osteophytes increase in size and especially the adductor portion of the head becomes disproportionate. In advanced cases the adductor osteophyte may be half as large as the head itself (Fig. 4b) and run

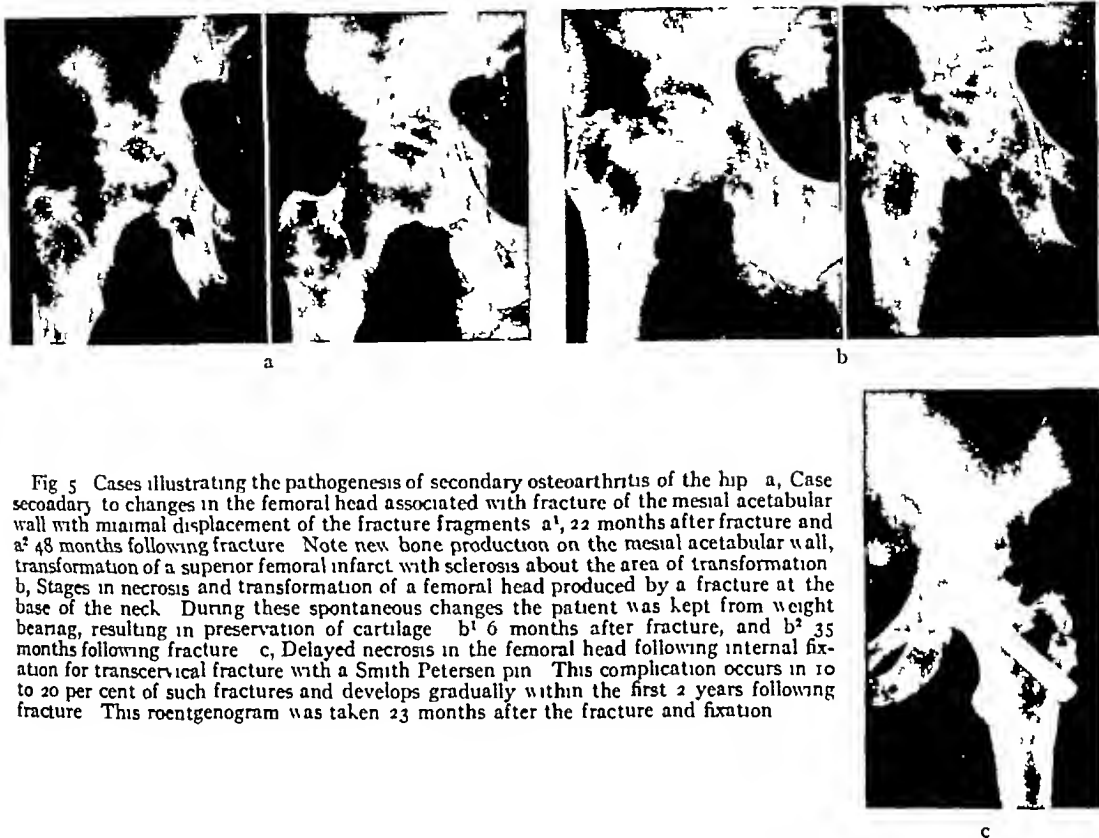


Fig 5 Cases illustrating the pathogenesis of secondary osteoarthritis of the hip a, Case secondary to changes in the femoral head associated with fracture of the mesial acetabular wall with minimal displacement of the fracture fragments a<sup>1</sup>, 22 months after fracture and a<sup>2</sup> 48 months following fracture Note new bone production on the mesial acetabular wall, transformation of a superior femoral infarct with sclerosis about the area of transformation b, Stages in necrosis and transformation of a femoral head produced by a fracture at the base of the neck During these spontaneous changes the patient was kept from weight bearing, resulting in preservation of cartilage b<sup>1</sup> 6 months after fracture, and b<sup>2</sup> 35 months following fracture c, Delayed necrosis in the femoral head following internal fixation for transcervical fracture with a Smith Petersen pin This complication occurs in 10 to 20 per cent of such fractures and develops gradually within the first 2 years following fracture This roentgenogram was taken 23 months after the fracture and fixation

cause partial dislocation of the head This portion of the head may render the femoral head egg-shaped and be a major factor in causing the head to be difficult to dislocate at operation and in restricting motion of the joint The head increases in size both by subchondral sclerosis and by its enlargement by osteophytic proliferation as just described Subchondral sclerosis is accompanied or preceded by the changes in cartilage as will be described As a result, irregular islands of cartilage thinning occur, which in advanced stages may bare subchondral bone Cartilage is thrown up into pleat and ridge formation, the whole giving the head an irregular appearance The extent of marginal overgrowth of bone and cartilage never parallels the rate of degeneration of cartilage over the head and of actual enlargement of the osseous structure of the head Consequently, osteoarthritic femoral heads are never identical

Most of the alterations which are seen in the customary anteroposterior roentgenograms of the hip and which appear to be acetabular osseous

overgrowths are actually alterations on or in the femoral head (Figs 4b and 11a) Indeed, such roentgenograms seldom give an accurate impression of the relative changes on the femoral head and acetabulum as actually visualized at operation Little or no removal of marginal overgrowths on the acetabulum is required except in advanced cases and then only from the anterior and antero-inferior portion of the acetabulum Lateral views of hip with leg abducted and externally rotated are of help in visualizing the extent of relative involvement of femoral head prior to operation

Avascular necrosis (2, 12, 21, 24, 26, 39, and 43) plays an important rôle in either initiating change in cartilage or else takes place in the femoral head after initial cartilage damage All femoral heads visualized and trimmed at operation in this series contained greater or smaller islands of osseous infarction The arrangement of these islands was often such as to suggest that wedge-shaped infarction either initiated the osteoarthritic changes or appeared at an early date in its course and contributed significantly to its advancement



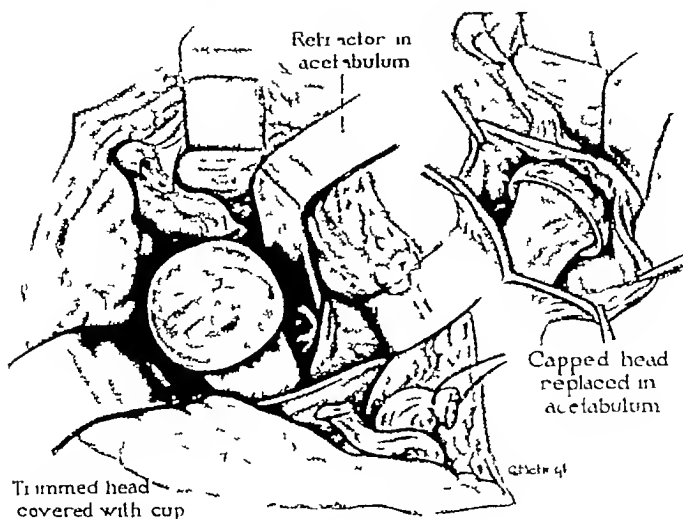


Fig 8 Capping the trimmed head and replacement of it into the acetabulum

These changes have been described by Axhausen, Phemister (34, 36), Kistler, Lang (24, 26), and others, to whose writings the reader is referred for details. The first change in the articular cartilage is a change in the staining reactions of the matrix which is the familiar gross increase in translucency and change in color. The matrix then becomes fibrillated, the direction of the cartilage pits being both vertical and horizontal. Deposits of calcium are seen in the cartilage, and pleats and cavities appear in the cartilage. The usual orderly arrangement of cartilage cells in articular cartilage is superseded by a "disordered appearance," and the viable cells are placed in an abnormal fibrous matrix. All transitions can be seen at times between normal cartilage and fibrocartilage.

Continued irritation of movement is probably responsible in some degree for changes that take place in subchondral bone. Beneath areas of cartilage change, osseous trabeculae thicken by appositional growth of osteoid tissue. The osseous subchondral plate itself thickens by the same process. Bony sclerosis also occurs by the process of enchondral ossification under areas that are better protected by cartilage. Proliferation of bone by the process just described occurs at the margins of the joint, and pushes cartilage before it, thus forming marginal osteophytes. The eburnated and polished appearance of subchondral bone is due to the tremendous thickening of this latter structure in addition to the polish it acquires by friction. Elsewhere, especially at

some depth beneath the osseous cortex, the trabecular pattern is thinned, and cyst-like structures containing fatty tissue are seen. Other cyst-like cavities (Fig 4a) are seen lined by fibrous tissue. The preponderance of these latter structures in certain cases has been responsible for the roentgenologist introducing the descriptive term of "senile cystic arthritis." It is but a type of degenerative arthritis.

#### ETIOLOGY AND PATHOGENESIS OF OSTEOARTHRITIS

Thirty-seven, or 39.4 per cent, of the 94 patients upon whom records were available at the Guthrie Clinic and the Robert Packer Hospital, could be assigned to the group of secondary osteoarthritis (Figs 3, 4, and 5). The remainder, including many in which wedge-shaped infarcts of the femoral head were present, was classed as primary. It is possible that, if roentgenograms had been made at earlier dates in some of the latter cases, many would have been placed in the category of secondary cases. The causes of secondary osteoarthritis of the hip are given in Table I, and some illustrations of this type are shown in Figures 2 to 5. These findings are in agreement with those of Plewes, Gilmour (14), and Wiberg. The first mentioned, in reviewing 242 cases from an English orthopedic hospital, found that in 47.9 per cent of his cases a definite preliminary disorder, often an adolescent hip joint disease, had caused enough damage to be later followed by osteoarthritis. Presumably the





Fig. 9. Case 4. Bone removed from the femoral head in the arthroplastic operation described in this report. The eight of these specimens, sizes from 50 to 80 grains, designates osseous fragments bearing remains of articular cartilage. Notch, pits and ridges.

early mechanical derangement subjected the hip to unusual weight bearing stress and caused early cartilage degeneration and the other changes previously described.

The mean age in the group of patients with primary osteoarthritis of the hip was 64 years while that of the secondary cases was 45 years. The incidence of osteoarthritic changes in other joints in the first group was four times as common as in the group of secondary cases. The disease was unilateral in all the secondary cases, except

those following posttraumatic acetabuli (Fig. 10), rheumatoid arthritis, Paget's disease and slipped upper femoral epiphysis (Fig. 11a). Osteitis of a significant degree was present in one third of the cases, and the body build in almost all the patients. Females included, could be described as "large." Foci of infection, generalized arteriosclerosis, cardiac disease, anemia and increase in the blood sedimentation rate were encountered occasionally but not with a frequency that could implicate them as causative of the condition. Indeed, save for the joint condition, the majority of these patients were of unusually good physical condition. All facts served to point to a degenerative disease of the hip, often preceded by a disorder that then subjected this structure to mechanical disadvantage. The bony changes that were encountered are the reactive changes in a joint that continues in the following initial damage. Magnusson and others have reached a similar conclusion in studying other joints affected by osteoarthritis.

#### OPERATIVE TECHNIQUE

When the hip joint is opened for an arthroplastic procedure in the presence of a movable joint, it is not necessary to carry out a radical dissection as is necessary when this joint is almost totally or completely ankylosed. In the instance of total osseous ankylosis as encountered in the end-stages of pyogenic arthritis of the hip joint or instances of ankylosis from the Marie Strömper



Fig. 10. Roentgenograms of the hip of Case 1. Preoperatively showing sclerosis, diminished joint spaces and small projecting adductor osteophyte that articulated with similar acetabular overgrowth and blocked abduction and rotation. Six months after operation. A portion of infarcted bone in the superior portion of the head, as noted. At operation this bone had been noted but there was no evidence of its separation. Eighteen months after operation. Note healing in the head and that the infarcted bone has separated and now lies in the inferior portion of the joint. The patient's motion has been maintained and he has had no pain or locking of the joint.

TABLE I—CAUSES OF SECONDARY OSTEOARTHRITIS OF THE HIP

Juvenile and adolescent
Coxa plana (Legg Calvé Perthes' disease)
Slipped (or slipping) upper femoral epiphysis
Septic arthritis (with or without dislocation)
Childhood arthritis (Still's disease)
Congenital dislocation of the hip (with or without operation and/or reduction)
Congenitally inadequate acetabulum
Congenital anomalies of the upper femur
Coxa vara of other types (rickets, osteomalacia, etc)
Adult
Injury (followed by aseptic necrosis in femoral head)
Fracture of the pelvis into the acetabulum
Fracture of the femoral neck
Traumatic dislocation, complicated by late avascular necrosis
Rheumatoid arthritis
Septic arthritis
Protrusio acetabuli (Otto pelvis), traumatic or infectious in origin
Paget's disease of pelvis and upper femur
Caisson disease
Chondromatosis and osteochondritis dissecans
Lues (painless "Charcot" hips)

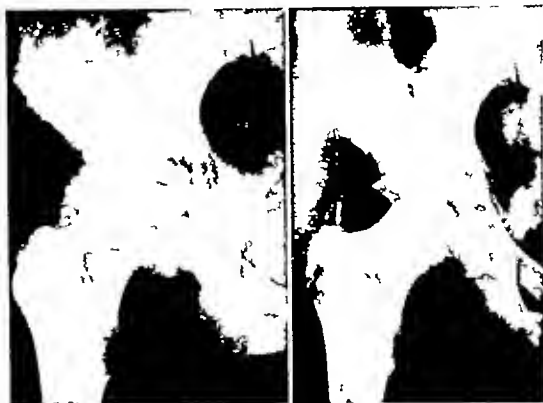


Fig 11 a, Preoperative roentgenogram of Case 6, secondary osteoarthritis following an adolescent slipped upper femoral epiphysis and aseptic necrosis in the femoral head. Motion at this time was limited to flexion only. b, Roentgenograms 6 months after operation. Note the improved mechanical condition of the hip and that nearly all excess bone was on the femoral head.

type of atrophic arthritis, the partial intrapelvic approach recently described by Smith-Petersen (44) should be used. It is seldom necessary to make such an extensive dissection in patients upon whom arthroplasty is being performed for osteoarthritis.

The technique recommended requires minimal detachment of muscles since it is felt that hip-joint motion is only further weakened by extensive dissection. An 8 to 10 inch horizontal incision is made in the upper anterior thigh, the upper 2 inches of which curves outward from the anterior superior iliac spine, along the anterior iliac crest (Fig 6, inset). This latter structure is exposed, and the subcutaneous incision is extended downward along the outer border of the sartorius muscle. The upper 4 inches of the sartorius is de-

fined, its origin removed, together with a fragment of cortical bone, from the anterior superior iliac spine. A portion of the origin of the tensor fascia lata and the extreme lowermost fibers of origin of the gluteus minimus are detached by subperiosteal dissection from the lower anterior iliac crest. Care should be taken to detach only the minimum of muscle in this last maneuver, it is never necessary to detach the fibers of the gluteus medius when the hip remains movable. The total length of the muscle detached from the iliac crest never need exceed 2 inches and is often less. By retracting the detached sartorius downward in the wound, the anterior inferior iliac spine is exposed, and the origin of the tendinous head of the rectus femoris is defined. It is then

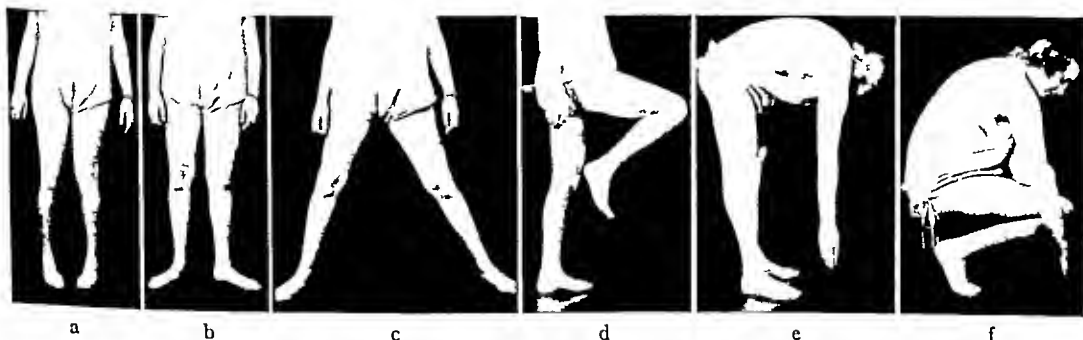


Fig 12 Photographs illustrating the range of active motion 9 months following operation in Case 6. a, In

ternal rotation, b, external rotation, c, abduction, d, flexion, e, bending, f, squatting.



Fig. 5 a, Preoperative roentgenogram of the pelvis of Case 2, bilateral primary (I) osteoarthritis of both hips. The acetabulum has some characteristics of arthralgia (Otto pelvis) which is reversible. b, better effect in b, the postoperative roentgenogram, taken 3 months after the operation. c, roentgenogram of the left hip, 5 months following cup arthroplasty showing collapse (partial) of the head neck steep and right bearing.

detached by cutting through the tendon. The distal free tendinous edge is anchored to the lower wound margin by transfixing it three or four times by a through and through stitch of No. 10 or chromic catgut and stitching it loosely and temporarily into the lower angle of the wound. This same stitch is later used to reattach the divided tendon of the rectus femoris upon conclusion of the operation.

The accurate placement of retractors at this point gives complete exposure of the anterior and superior portions of the hip-joint capsule. Both bands of the iliofemoral ligament should be visible in their entire course. The iliacus is retracted medially with a broad retractor, the tensor fascia femoris laterally and posteriorly, and the gluteus minimus and the lower border of the gluteus medius superiorly. The detached sartorius and rectus femoris are in the inferior angle of the wound (Fig. 6). The ascending terminal branch and 1 to 2 times the transverse terminal branch of the lateral circumflex artery are usually exposed. Time is conserved and better hemostasis is obtained by dividing and ligating the vessels if they lie near the surface over the anterior aspect of the hip-joint capsule. There is much variation in the origin, course and branches of the lateral circumflex artery, but they can be visualized. The capsule is then opened by

crucial incision. The extent of periacetabular new bone is noted, and the necessary amount is removed from the anterior acetabular margin. The femoral head is then dislocated. This maneuver is facilitated by driving a slightly curved broad bladed osteotome into the anterior aspect of the joint between head and acetabulum. The operator levers the head out while an assistant manipulates it externally. Both the femoral head and the interior of the acetabulum are then thoroughly inspected and the extent and nature of the pathological changes are noted. The ligamentum teres will usually be found absent or represented by a well compressed fibrous cord. Cartilage destruction is usually most accentuated on the weight bearing portion of the femoral head, and is usually farther advanced over the femoral head than in the acetabulum. When osteophytic bone is the prominent feature of the pathological process, it is distributed circumferentially about the femoral head, extending distally back over the neck, especially on the superior and anterior aspects. The cortical bone of the neck is often obscured. The head in osteoarthritis is usually distorted in shape by osteophytes, especially the adductor enlargement which is an almost constant and important part of the pathological picture.

The femoral head should be reduced to a volume definitely smaller than normal circumferential size. Often one-third to one-half of the mass of the pathological femoral head is removed inasmuch as it usually is increased in size (Figs 7, 10, and 11). The amount of bone removed averages from 50 to 80 grams. Osteophytes are trimmed from the head-neck margins, a plane of division being easily found between these new-growths and the normal cortical bone of the neck. All types of osteophytic variations will be found from a marginal ring at the head-neck margin to gigantic osteophytes that bridge the entire neck and are contiguous with trochanteric bone. When wedge shaped areas of osseous necrosis are present in the femoral head, they are easily recognized by the yellow avascular appearance contrasting to bleeding bone about them. The head is reshaped without special attention to them, except to reduce the total head volume to the minimum in this special instance and thus to shorten the longitudinal neck diameter. Care must be taken to trim the head symmetrically in relation to the neck, since the osteoarthritic changes have usually rendered it asymmetrical.

Periacetabular osteophytes are removed by a curved chisel from an extra-acetabular approach. Since they frequently develop in the origin of the iliofemoral and pubocapsular ligaments, portions of the acetabular attachments of these ligaments are frequently torn in their removal. No special attempt is made to reattach the ligaments. If the detachment is extensive, portions of the ligaments are excised, but since removal of periacetabular bone is seldom extensive, a fair reconstruction of the capsule can be obtained and is recommended. The acetabular surface is not attacked unless it is extensively ridged by cartilage pleats and by islands of surviving cartilage, in which case, the osteocartilaginous surface is carefully smoothed by shaving off excess cartilage. Bone removed and some of the surface changes are illustrated in Figure 9.

The presenting and raw osseous surface of the reduced femoral head is then smoothed with the cup reamer and capped by a loosely fitting methacrylate hemisphere. In most of our cases, the two smaller size cups were the best fits. Care should be exercised that the cup is quite loose over the head and that the cup does not bind in the acetabulum after reduction of the dislocated head (Fig. 8). The capsule is then closed loosely with interrupted fine cotton sutures. The muscles are reattached with the same suture material, the deep fascia is closed with interrupted cotton sutures, and the subcutaneous tissues are approxi-

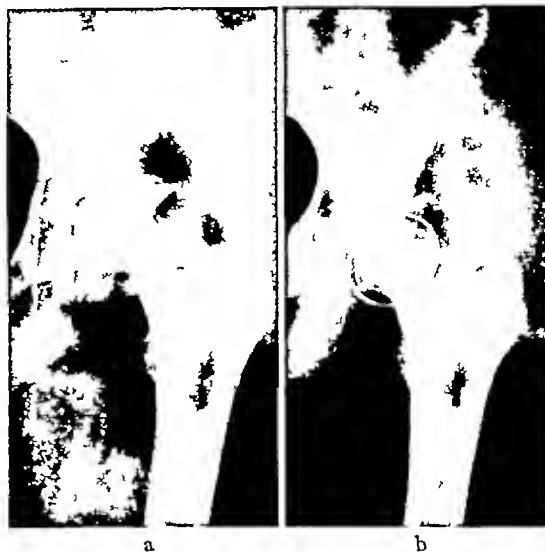


Fig 14 a, Preoperative roentgenogram of Case 9, osteoarthritis secondary to possible juvenile pyogenic arthritis. In this instance the new bone is both acetabular and from the head neck junction. Note the large superior osteophyte and the moderate sized adductor osteophyte. b, Postoperative roentgenogram. Note that the acetabulum is deformed, its cavity opening more anteriorly than antero-inferiorly.

mated by the same method, with care to bury the knots well beneath the skin. The skin can then be approximated by any of the recognized methods.

#### POSTOPERATIVE TREATMENT

For the first 2 to 3 weeks the limb is held by an internal rotation strap of broad adhesive and by Buck's extension (7 pounds) applied to the leg. The balanced Hodgen or Thomas splint with a Pearson attachment can be used for limited active and passive motion to both hip and knee. Both are started within a few days after operation, as soon as the muscle and wound tenderness will permit. During the third week, Buck's extension is used intermittently for a week and the patient is up in a wheel chair and begins systematic exercise in the physiotherapy department. Active and passive exercises are then given daily for both hip and knee. The patient is instructed to devote 10 minutes of every waking hour to combinations of quadriceps setting exercises, and active flexion and abduction of the hip. There is no danger of dislocation of the hip. The patient is allowed to walk with the aid of crutches, supporting body weight largely on the normal leg, from 25 to 28 days after operation. Full weight bearing



b



d

Fig. 5. Preoperative and postoperative roentgenograms from two additional bilateral cases—Cases 7 and

8. a and c, are preoperatively; b and d are film taken following operation.

on the operated leg is allowed, still with crutches, 4 to 7 weeks after operation. The patient is requested to continue to use crutches until he has full confidence in the strength of the hip that has been operated upon. The use of crutches is insisted upon for 3 months following operation upon a single hip, but upon request some of the patients have not discarded them until 4 or 5 months after operation. Careful postoperative manipulation is occasionally used to increase motion but the majority of cases do not need it. It should always be performed gently. When both hips are operated upon the same patient, the second hip is usually done some 10 days to 2 weeks after the first. With the patient in bed physical therapy is then given to the hip joint first operated upon until the second hip is removed temporarily from traction. After the 4th week in the case of unilateral operations and the 6th week in bilateral

operations, strenuous exercise upon the bed-tilt plane and upon the exercising bicycle is given.

#### REPORT OF CASES<sup>1</sup>

**CASE 1.** Male, aged 60 years, suffered from osteoarthritis of the left hip for 15 years prior to treatment at the Robert Packer Hospital and Gethsemane Clinic. Marked pain was present in the left hip during the year prior to operation. The limit of his endurance in walking was one or two blocks. At operation plastic cup was inserted in the hip and the femoral head was reduced and fixed in place. The patient's postoperative course was unremarkable but he continued to use crutches, on our recommendation for 4 months. The postoperative range of passive motion double that prior to operation. From the 10th month the patient stated that he could walk 3 to 5 miles daily without pain. During the changeable winter months, however, he complained of "muscle soreness" of short duration in the left thigh (referred pain). It was considered that the patient had almost complete relief from pain. Roentgenograms of the patient are reproduced in Figure 10.

<sup>1</sup>Table II shows for all cases range of passive motion before and after operation. (A.C. motion, in table, was three-fourths passive.)

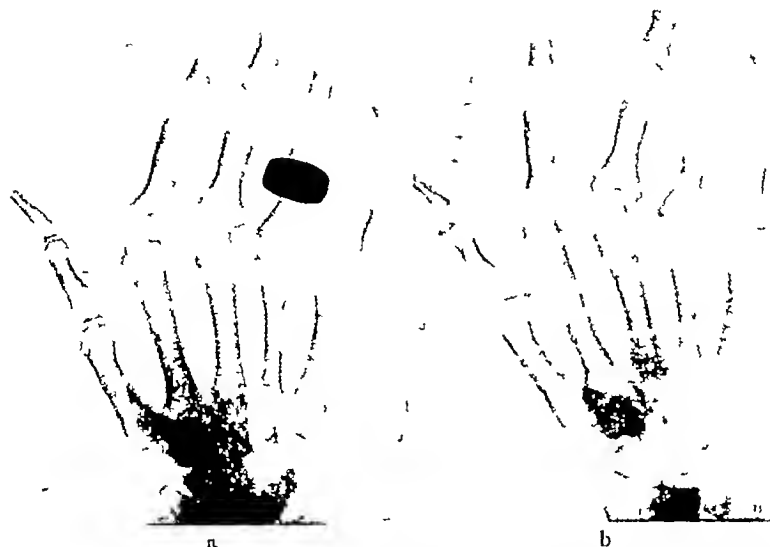


Fig 16 Roentgenograms before, a, and after operation, b. Note the restoration of joint space and the trimmed distal fourth metacarpal head in the latter view

**CASE 2** Male, aged 60 years, suffered from multiple osteoarthritis chiefly affecting the lumbar spine and the left hip, although there were definite changes in the right hip and in both knees. The duration of this process was 2 to 4 years prior to operation. In the 4 months prior to operation he had had 6 or 7 acute attacks of pain in the right hip which necessitated his being off work for several days on each occasion. At operation on the right hip, marked changes of degenerative osteoarthritis and many marginal osteophytes were found on the head. The bone of the femoral head was eburnated and avascular, the latter changes extending into the head in multiple wedges. One third of the entire mass of the head was trimmed away, with no attention to the distribution of avascular bone. The hypertrophied superior and anterior ledges of the acetabulum were removed with a chisel from an intracapsular approach. In this case the remains of the ligamentum teres were present and a slight ooze was identified from the proximal end of this structure, after dislocation. Following operation, the patient has never been able to walk without his crutches, except in his house. He has had two or three attacks of pain in the opposite hip and in both knees, although the hip on which the arthroplasty was performed has been the site of greatly increased motion and he has been relieved of pain in this hip.

This case is now considered as being an error in selection (age, poor muscle strength, and multiple osteoarthritic involvement, the symptoms of which are moderately active at the present time).

**CASE 3** Male, aged 40 years, dated the onset of his disability to World War I. While in the armed forces he received an injury to his hip without fracture. He had always had some pain and disability in the hip during the 20 years succeeding the injury, but these symptoms had become gradually worse during the 4 or 5 years prior to being seen

at the Guthrie Clinic and the Robert Packer Hospital. Roentgenograms showed far advanced osteoarthritis of the left hip (secondary). The joint space was almost completely obliterated and there were large osteophytes both on the margins of the acetabulum and the femoral head as well as sclerosis and small cysts within the head. During the immediate 1 year prior to operation the pain had been considerable most of the time and had forced the patient to resort to alcohol and to crutches for relief. At operation, a large number of periacetabular osteophytes were seen and removed, especially from the anterior and inferior margins of the acetabulum. The bone of the head and trochanter was united over the anterosuperior portion of the trochanter by an osseous bridge. It was estimated that the head was trimmed to one half its previous proportions. The weight of the bone removed at operation was 82 grams. In the outer third of the head a large quantity of avascular bone was encountered during the trimming process. The head was then capped with a plastic cup, after it had been smoothed with a female reamer. Following operation, the patient progressed according to schedule and was discharged 5 weeks after operation. Further postoperative course was ideal, except for one bout of an acute exacerbation in the right hip occurring 4 months after operation. At that time, against our advice, he had gone without his crutches for 2 weeks and had participated in some unusual exercises. The pain again disappeared following great restriction in his activities. Fourteen months after operation the patient reported, on a follow up visit, that he was on his feet 8 to 12 hours per day and suffered no pain. Active motion was about  $\frac{3}{8}$  of the range of passive motion (Table II).

**CASE 4** Female, aged 64 years, had begun to suffer pain in the right knee (referred pain from the right hip) 8 years prior to admission to the Guthrie Clinic and the Robert Packer Hospital. On admission the patient had markedly restricted motion at the right hip (Table II) which was

TABLE II.—RANGES OF PASSIVE MOTION AT THE HIP JOINT BEFORE AND AFTER METHACRYLATE CUP ARTHROPLASTIES

(In degrees, from neutral position; time postoperatively in months)

Case No.	Sex Age		Flexion	Extension	Total abduction Total adduction	Rotation	Comments
	M 66	Preoperative	30		75	10	Excellent
		Postoperative (25 mo.)	60	30	30	20	
	M 66	Preopnd	70				Poor
		Postoperative (16 mo.)	30	20		20	
	M 30	Preopnd	60	10			Excellent
		Postoperative (1 mo.)	30	20		30	
	F	Preoperative	30				Poor
		Postoperative (month)	60	10	30		
		Postoperative (11 mo.)	70	20	20	15	
	F 43	Preopnd	60	20	60	10	Excellent
		Postoperative (12 mo.)	30	30	20	20	
6*	F 34	Preoperative	60				Excellent
		Postoperative (1 mo.)	30	30	20	30	
7	M	Right, preopnd	30				Good
		Right, postoperative (11 mo.)	30	10	30	10	
		Left, preoperative	30				
		Left, postoperative (1 mo.)	30	20	30	10	
8†	27	Right, preoperative	60				Poor to fair
		Right, postoperative (15 mo.)	60	20	70	20	
		Left, preopnd	30				
		Left, postoperative (15 mo.)	30	20	70	20	
	F 30	Preoperative					Excellent
		Postoperative (14 mo.)	60	20	10	60	
10	M 39	Right, preopnd					Fair
		Right, postoperative (1 mo.)	30	20			
11	F 53	Right, preopnd	60				Excellent
		Right, postoperative (13 mo.)	75	20	50	30	
12†	44	Preoperative	65	10	60		Excellent
		Postoperative (20 mo.)	70	30	60	30	
13	30	Right, preopnd	20		20		Excellent
		Right, postoperative (1 year)	60	10	70	20	
		Left, preoperative	30				
		Left, postoperative (17 mo.)	60	30	70		

\*1 degree flexion contracture.

30 degree flexion contracture each hip.

14 degree flexion contracture each hip.

1 degree flexion contracture.

30 degree flexion contracture at left and 1 degree at right hip.

always guarded by muscle spasm and pain. Arthrotomy was performed under spinal anesthesia. When the femoral head was dislocated it was found that there was an extensive system of periacetabular osteophytes present, but the cartilage was in fair condition, being the least degenerated and worn of any of the cases in this series. The head was trimmed about one third, capped with a hollow plastic hemisphere, and replaced. The patient's postoperative course was prolonged somewhat requiring her to remain in the hospital for 10 weeks following operation. Convalescence was further complicated by a slight but persistent anemia (hemoglobin 58 to 65 per cent, red blood cells, 2,300,000 to 3,700,000 per cubic millimeter). Diet, hematonic drugs, and transfusions appeared to influence the anemia but little. Convalescence was further prolonged by the patient developing lymphedema of both lower extremities below the knees. This latter was partially controlled by Unna's paste boots. Following the operation, this patient has been able to get about only with the aid of crutches, largely because of the complications noted

This case is considered a poor result because of the nonorthopedic complications, although a good mechanical result was secured in the hip. This case is also considered a poor selection (age, persistent anemia, muscle weakness, and edema of both lower extremities).

CASE 5. Female, aged 45 years, stated that when she was 9 years of age she had fallen from a roof injuring her hip. This was followed by a prolonged convalescence. There had always been some pain in the hip from that time (secondary osteoarthritis). Fifteen years prior to operation the pain reached an annoying point and had been gradually progressive during this latter period. Prior to operation she could walk only one or two blocks due to pain and disability of the hip. At operation, a slab of bone 1.5 by 1 centimeter was found in the anterior portion of the capsule. The hip was found to be blocked in abduction by articulating osteophytes on the one side from the head and on the other side from the cervicotrochanteric region. After dislocation, the head was found to be egg shaped, the large adductor osteophyte being one portion of the mesial projection of the head. The head was reduced to about one half its former volume, capped with a hollow plastic hemisphere, and replaced. The range of postoperative motion is shown in Table II. The patient has been entirely relieved of pain but continues to have a slight gluteal gait which has been greatly improved by a 0.5 inch lift on the shoe heel of the leg operated upon.

CASE 6. Female, aged 29 years, had had pain and stiffness in the right hip for 12 years prior to operation. On careful questioning the patient stated that "hip joint disease" had been diagnosed at the age of 12 and that roentgenograms had been made of the hip 10 years prior to the time she consulted me at the Guthrie Clinic and the Robert Packer Hospital. These roentgenograms were available for inspection and showed some changes in the hip which were probably those of an ancient slipped upper femoral epiphysis, and secondary osteoarthritis (Figure 11). A large wedge shaped infarct was located in the head. This infarcted area had remained almost unchanged in roentgenograms through the 10 year period. Physical examination showed that the right hip had been converted into a hinge joint (Table II). At operation a large ledge of sclerotic acetabular new bone was found to project anterolaterally. A large exostosis from the femoral head articulated with a corresponding structure originating from the trochanteric region, explaining the patient's lack

of rotation and abduction. After dislocation of the head, this structure was found to be wedge shaped, and the relation of the neck to the head was greatly distorted. The head was trimmed to half its former volume, 50 grams of bone being removed. The head was then capped with a plastic cup and replaced. The capsule was loosely reconstructed with interrupted sutures of silk. The patient made a very rapid recovery from the operation and discarded crutches 3 months later. When last seen 13 months following the operation, the range of motion in the diseased hip was practically normal (Fig. 12). The patient complained of no pain and had been extremely active for many months on it.

CASE 7. Male, aged 47 years, stated that 10 years prior to being seen in the Guthrie Clinic and the Robert Packer Hospital he had had an acute attack of multiple arthritis which had left both hips fairly stiff. However, he had been able to get around with little aid except from canes until 1½ years prior to admission. At that time the pain had become so severe and continually disabling that he had remained in bed for 1½ years prior to admission.

Upon examination, both lower extremities were found to be almost fixed in 45 degrees' external rotation and slight flexion (bilateral osteoarthritis, secondary to atrophic arthritis). There was no motion at any plane about the hip except 20 to 30 degrees in flexion. Plastic cup arthroplasties were performed on both hips, 10 days elapsing between operations. The findings in both hips were similar. There was a very fine line of osteophytic bone projecting from the anterior, superior, and inferior portions of the acetabular head. On both sides the femoral head was ovoid in shape. Islands of avascular bone were found in both, in addition to cartilage degeneration. Both femoral heads were reduced about one half in volume, 50 grams of bone being removed from the left hip and 55 grams from the right. The patient was discharged walking with crutches 2 months following the last operation. This patient's preoperative and postoperative courses were complicated by obesity which limited his postoperative exercises somewhat. While the patient has been unable to be ambulatory without the aid of crutches during the year succeeding the operation, the range of motion in the hip has been doubled and he has secured motion in abduction and rotation, and he has been converted from a bedridden patient to an ambulatory one. The outlook is that he will continue to need crutches, but there is no evidence of restriction of motion during the year following the operation. He has complained of no pain during the 10 months he has been fully ambulatory following operation.

CASE 8. Female, aged 37 years, stated that she had been in good health prior to 1½ years before admission, when she began to suffer intermittently from pain in both feet. She had suffered intermittently from pain in both knees, both ankles, and both hips during the interval mentioned but during the 1½ years prior to admission her disability was chiefly that present in both hips. Roentgenograms (Fig. 13a) showed osteoarthritis of both hips. Plastic cup arthroplasties were performed on either hip, the operations being spaced at an interval of 3 weeks. Changes found in the hips were similar on the two sides, there being an extremely deep acetabulum present (Figure 13b). Osteophytic new bone had proliferated about the superior and anterior margins of both hips. The dislocated head was trimmed to about one half its previous volume, most of the bone being removed from the inferior and mesial portions of this structure. Eighty grams of bone were removed from each hip, and the patient was discharged from the hospital 6 weeks following the second operation. During the succeeding 9 months she has maintained the amount of passive and active motion present upon discharge. This patient, however, has complained intermit-



tently of pain in both knees and in the right hip, the former being present to greatest extent during the month following the operation on her hip. The patient also has complained somewhat of muscle pain in the right thigh (referred pain). The left hip has been entirely asymptomatic. This patient is considered as completely relieved of pain in the left hip and markedly relieved of pain in the right one. The symptoms in the latter are associated with the progressive collapse of the thinned head and neck (Fig. 3c). The transparent plastic cup has allowed correct evaluation of the cause of failure to relieve pain in the right hip.

**CASE 9.** Female, aged 30 years, as entirely ill until the age of 4 years, at which time she was taken by Scheffle disease accompanied by acute pain in the right shoulder and left hip. At that time she was confined to bed for 4 months, and no operation was performed on the hip. Roentgenograms made then showed an "infected hip," but these films are not available to us. The patient had suffered so much pain in the left hip that she had been using crutches for 7 years and had markedly restricted her activities 1 year prior to this time (osteoarthritis, secondary to juvenile pyogenic arthritis). At operation, an extensive anterior erosion of the head and neck, as found. A large mass of osteophytic new bone was found inferiorly and anteriorly and three large size adductor osteophytes were found on the head (Fig. 4). The head was trimmed to one-half its previous volume, and the osteophytes were removed from the head and the neck. The head was capped with plastic cup and replaced. Total weight of bone removed was 55 grams.

This patient has had an excellent postoperative course, being discharged 30 days following operation. Increase in postoperative motion in her hip has been gradual but progressive especially during the past 6 months. She has been totally relieved from pain.

**CASE 10.** Male, aged 59 years, stated that he had had attacks of pain in both hips at the age of 45 years at which time he was living Gratz, Austria. He stated that he has had some pain and disability in both hips intermittently since that time but both hips have been more painful during the past 3 years. Marked restriction of motion had been noted during the previous 3 years. On admission to the Guthrie Clinic and the Robert Packard Hospital, there was only slight amount of motion in either hip, both of which were held in about 45 degrees external rotation.

At operation, extensive difficulty was experienced in dislocating the right hip. This was explained by the complicated and ramifying system of adductor osteophytes. This complicated osteophytic projection as about two-thirds the size of the femoral head, projecting into similar irregular erosion in the acetabulum. Following dislocation of the hip, this structure was trimmed to one-half its previous volume, capped with plastic hemisphere, and replaced.

The patient's postoperative course was slow. This patient has never developed motion in the right hip comparable to that in other cases.

This is graded as only a fair result and is now considered to be in error in selection (age, muscle weakness, bilateral extensive involvement).

**CASE 11.** Female, aged 55 years, had foot pain and disability in both hips 3 years prior to admission to the

Guthrie Clinic and the Robert Packard Hospital. During the 3 years previous to admission the left hip had been progressively stiffening and on admission there was no detectable deformity in it.

Plastic cup arthroplasties were performed at 4 month intervals. During the interim there had been special in the left hip, the site of the first operation. This hip was explored 6 weeks following the second arthroplasty. It was found that tight scar tissue band had bridged the inferior acetabular notch. The aponeur was separated and appeared to originate from the band. Section of it abolished the aponeur and it has not returned following exploration. Findings in both heads were similar, as an unusually large ledge of acetabular new bone had grown from the superior and anterior margins of the acetabula (Fig. 5). Islands of vascular bone were found both femoral heads. Cartilage of both heads was so slightly degenerated but markedly ridged and pitted. The patient was almost totally relieved from pain following operation.

**CASE 12.** Female, aged 44 years. Disability began in the left hip at the age of 3 years (osteoarthritis of the left hip, secondary to slipped upper femoral epiphysis).

Examination of the left hip on admission to the Guthrie Clinic and the Robert Packard Hospital showed no degeneration deformity of the left hip and other present status as noted in Table II. At operation, large ledge of osteophytic new bone was found anteriorly and superiorly on the acetabulum. There was large trough of new bone which originated chiefly at the inferior portion of the head and extended around three-fourths the circumference of this structure. The osteophyte on new bone was trimmed and the volume of the femoral head was reduced to about one-half its previous volume. Cartilage was very thin, and the weight of new bone removed was 45 grams. This patient had good postoperative course.

**CASE 13.** Female, aged 30 years, had been seen on several occasions in the Guthrie Clinic and the Robert Packard Hospital over a period of several years, prior to admission. Plastic cup arthroplasties were performed on both hips at 4 month intervals. The findings in both hips were similar. The lateral surface of the femoral head was severely biconcave due to the structure having sunk into the acetabulum (Fig. 5). There was little evidence of erosion new bone on the acetabulum except for moderate amount on the anterior and inferior portions. After both hips were dislocated, extensive cartilage degeneration was noted. Plastic cups were fitted to the femoral head, and the femur reduced into the acetabulum. The postoperative course was excellent, and the patient had complete relief of pain in both hips.

#### ANALYSIS OF STUDY

The results in this series of cases have been encouraging. While motion has been restored in most of the cases, such a result is secondary in importance to relief of pain. The end-results of increase in motion in the hip joint are to some extent dependent upon the amount of motion originally present. It is seldom that more than 45 degrees of passive flexion can be obtained by operation in the average osteoarthritic hip of several years duration when only a few degrees of motion are present prior to operation. Such cases are usually in the older age groups and, either due to this or other factors, have poor results.

withdrawing 9.5 cubic centimeters of blood into a syringe containing 0.5 cubic centimeter of a 1:100 dilution of heparin. In order to prevent clotting of the unmodified blood the syringe, previously chilled, was coated with mineral oil and the blood immediately transferred to paraffin-lined test tubes packed in ice. The blood was centrifuged for 5 to 7 minutes at 2750 revolutions per minute in large metal cups filled with ice.

In some of the early experiments lung extract was used to promote clotting of the plasma. The lungs of a small mouse were removed aseptically, washed with a small amount of physiological saline solution, minced, and then ground in a mortar with the addition of 10 drops of normal saline solution. The suspension was then centrifuged and the clear supernatant fluid used as the clotting agent. It was thought that autologous tissue extract as the clotting agent might lessen the local postoperative reaction, and muscle was investigated for this purpose. Although muscle extract was not as efficacious as lung extract in inducing rapid clotting, satisfactory results were obtained when the muscle extract was prepared in a specially concentrated form. The tissue was removed from the gluteal region about 2 centimeters above the site of the proposed nerve suture and the precaution was taken to keep the traumatized area separated from the sciatic nerve by intact muscle. A piece of muscle weighing about 2 grams was excised, minced, and ground in a mortar with sand and 7 to 10 drops of normal saline solution. The suspension was revolved at maximum speed in an angle centrifuge and the supernatant fluid was then removed by pipette.

The technique of performing the nerve suture in rabbits consisted in bringing the retracted stumps together by means of fine jeweler's forceps, depressing the junction into the fascial and muscle bed so as to form a trough, and adding first 5 drops of plasma and then 1 drop of tissue extract. The fluids were thoroughly mixed *in situ* and then about 2 to 3 drops of the mixture were withdrawn into a pipette to reduce to a minimum the amount of clot remaining as suture material. Although clotting occurred in about 40 seconds the nerve ends were held together with the forceps for about 4 minutes to make certain that the clotting process was complete. After release of the forceps, separation at the suture site frequently occurred. Usually the clot was removed after such separation and the procedure was repeated.

Silk suture of the sciatic nerve was done in some cases for the purpose of comparing the resultant tissue reaction with that which followed plasma clot suture. The technique of the silk

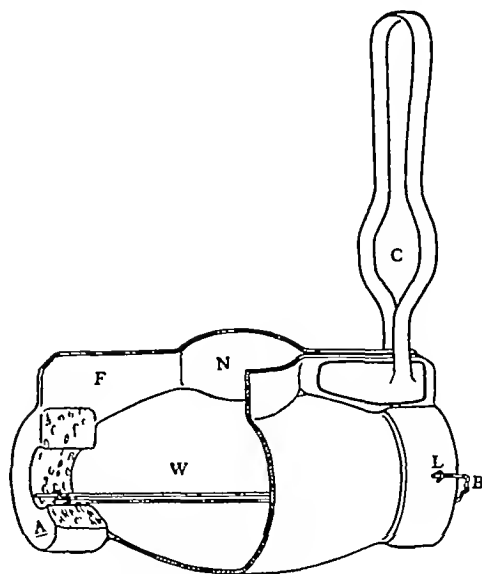


Fig 1 Sketch of latex mold used for plasma clot suture of nerves. *W* represents wire supporting rails which prevent sagging of the nerve ends. The rails (No. 34 nickel silver), which are removable, are threaded through wire loops in the base of the air foam collar, *A*. The handle, *B*, of each rail is held in place by a wire loop, *L*. Metal clips, *C*, are applied to the fins, *F*, of the mold. The clips serve to tighten the grip of the air foam collars and thus prevent retraction of the nerve as well as leakage of plasma. Plasma is introduced into the mold through the funnel, *N*.

suture consisted in using 2 silk stitches on opposite sides of the junction. Each suture consisted of 1 of the 3 component strands obtained by unravelling fine number 4 silk. An attempt was made to confine each stitch, so far as possible, to the nerve sheaths.

Usually both sciatic nerves were cut and different suture material was used on the two sides. In a few instances the nerve was cut, and the ends were held together for 4 minutes as for clot suture but were not actually sutured. In a few other instances, nerve suture was attempted with whole blood. Closure of the wound was carried out in a uniform manner in all cases. Interrupted fine silk sutures were used in the fascia covering the muscle and the skin edges were approximated with continuous fine silk sutures.

More recent experiments have been carried out in dogs. The experiences gained from the operations in rabbits made it clear that the surgical technique employed in these animals was inadequate. One of the most serious difficulties lay in the fact that the procedure of holding the nerve ends in apposition at the base of a trough formed by the neighboring tissues permitted the added

TABLE I.—INCIDENCE OF SEPARATION AND DEGREE OF HISTOLOGICAL REACTION ASSOCIATED WITH VARIOUS TYPES OF NERVE SUTURE IN RABBITS

Type of suture	No. of operations	No. of operations in which separation of nerve ends was observed following suture		Intensity of tissue reaction showing number in each group*			
		Immediately at operation	Later at autopsy	+	++	+++	+++
Rabbit plasma clot							
Unmodified				3			
Heparinized	20						
Citrated							
Total							
Human plasma clot							
Unmodified							
Heparinized							
Citrated							
Total							
Cochlear plasma clot							
1 Fertilized							
1 Unfertilized							
Total							
Whole blood							
A.R.							
*Nerve cut but not sutured	3	3		3			

\*plus represents successful and plus subnormal amount of inflammatory and fibrous reaction. †Cochlear nerve includes nerves

plasma to coat only one side of the nerve junction. To overcome this objection the technique was modified in the experiments in dogs. In these animals suture of the nerve was carried out in a rubber mold designed to retain the plasma at the suture site so as to produce a clot completely and uniformly surrounding the nerve junction.

The mold which was used in our early operations in dogs was made of latex in the form of a hollow tube wide open along its entire length and with a cup shaped depression in the center. Its chief fault lay in the fact that it did not provide for a adequate coating of the superior surface of the nerve. After the central cup was filled, any additional plasma tended to escape from the ends of the mold. A spherical latex mold with sleeves attached to envelop the nerve ends was used in subsequent operations. An opening was cut in the top of the mold to permit manipulation of the nerve stumps and introduction of the plasma. A slit extending from the opening to the ends of the sleeves was made to allow for the application and removal of the mold. Leakage of plasma at the sleeve ends still occurred occasionally since the size of the nerves which were sutured varied. A number of modifications of the spherical mold were made. A sketch of the mold which was used

in a few of the more recent operations, the results of which are included in this report is shown in Figure 1.

The technique in other respects was essentially similar to that employed in the operations on the rabbits except that nembutal was used as the anesthetic, the nerve was cut with a sharp scalpel and silk sutures of nerves were performed with the use of 4 rather than 5 stitches. After the nerve was cut, less retraction of the stumps occurred in the dog than in the rabbit. Seven to 15 drops of homologous or autologous plasma were used and clotting was either allowed to occur spontaneously or was induced by addition of autologous muscle extract or rabbit citrate globulin. After complete clotting had occurred the rubber mold was carefully peeled away and removed. As in the case of the rabbits, no attempt was made to immobilize the limb after operation.

Specimens of nerve were obtained at the 1st, 2nd, 4th, 7th, 10th, 14th, 21st, 28th, 35th, 42nd, 49th, 56th, 63rd, 70th, 77th, 84th, 91st, 98th, 105th, 112th, 119th, 126th, 133th, 140th, 147th, 154th, 161th, 168th, 175th, 182th, 189th, 196th, 203th, 210th, 217th, 224th, 231th, 238th, 245th, 252th, 259th, 266th, 273th, 280th, 287th, 294th, 301th, 308th, 315th, 322th, 329th, 336th, 343th, 350th, 357th, 364th, 371th, 378th, 385th, 392th, 399th, 406th, 413th, 420th, 427th, 434th, 441th, 448th, 455th, 462th, 469th, 476th, 483th, 490th, 497th, 504th, 511th, 518th, 525th, 532th, 539th, 546th, 553th, 560th, 567th, 574th, 581th, 588th, 595th, 602th, 609th, 616th, 623th, 630th, 637th, 644th, 651th, 658th, 665th, 672th, 679th, 686th, 693th, 700th, 707th, 714th, 721th, 728th, 735th, 742th, 749th, 756th, 763th, 770th, 777th, 784th, 791th, 798th, 805th, 812th, 819th, 826th, 833th, 840th, 847th, 854th, 861th, 868th, 875th, 882th, 889th, 896th, 903th, 910th, 917th, 924th, 931th, 938th, 945th, 952th, 959th, 966th, 973th, 980th, 987th, 994th, 1001th, 1008th, 1015th, 1022th, 1029th, 1036th, 1043th, 1050th, 1057th, 1064th, 1071th, 1078th, 1085th, 1092th, 1099th, 1106th, 1113th, 1120th, 1127th, 1134th, 1141th, 1148th, 1155th, 1162th, 1169th, 1176th, 1183th, 1190th, 1197th, 1204th, 1211th, 1218th, 1225th, 1232th, 1239th, 1246th, 1253th, 1260th, 1267th, 1274th, 1281th, 1288th, 1295th, 1302th, 1309th, 1316th, 1323th, 1330th, 1337th, 1344th, 1351th, 1358th, 1365th, 1372th, 1379th, 1386th, 1393th, 1400th, 1407th, 1414th, 1421th, 1428th, 1435th, 1442th, 1449th, 1456th, 1463th, 1470th, 1477th, 1484th, 1491th, 1498th, 1505th, 1512th, 1519th, 1526th, 1533th, 1540th, 1547th, 1554th, 1561th, 1568th, 1575th, 1582th, 1589th, 1596th, 1603th, 1610th, 1617th, 1624th, 1631th, 1638th, 1645th, 1652th, 1659th, 1666th, 1673th, 1680th, 1687th, 1694th, 1701th, 1708th, 1715th, 1722th, 1729th, 1736th, 1743th, 1750th, 1757th, 1764th, 1771th, 1778th, 1785th, 1792th, 1799th, 1806th, 1813th, 1820th, 1827th, 1834th, 1841th, 1848th, 1855th, 1862th, 1869th, 1876th, 1883th, 1890th, 1897th, 1904th, 1911th, 1918th, 1925th, 1932th, 1939th, 1946th, 1953th, 1960th, 1967th, 1974th, 1981th, 1988th, 1995th, 2002th, 2009th, 2016th, 2023th, 2030th, 2037th, 2044th, 2051th, 2058th, 2065th, 2072th, 2079th, 2086th, 2093th, 2100th, 2107th, 2114th, 2121th, 2128th, 2135th, 2142th, 2149th, 2156th, 2163th, 2170th, 2177th, 2184th, 2191th, 2198th, 2205th, 2212th, 2219th, 2226th, 2233th, 2240th, 2247th, 2254th, 2261th, 2268th, 2275th, 2282th, 2289th, 2296th, 2303th, 2310th, 2317th, 2324th, 2331th, 2338th, 2345th, 2352th, 2359th, 2366th, 2373th, 2380th, 2387th, 2394th, 2401th, 2408th, 2415th, 2422th, 2429th, 2436th, 2443th, 2450th, 2457th, 2464th, 2471th, 2478th, 2485th, 2492th, 2499th, 2506th, 2513th, 2520th, 2527th, 2534th, 2541th, 2548th, 2555th, 2562th, 2569th, 2576th, 2583th, 2590th, 2597th, 2604th, 2611th, 2618th, 2625th, 2632th, 2639th, 2646th, 2653th, 2660th, 2667th, 2674th, 2681th, 2688th, 2695th, 2702th, 2709th, 2716th, 2723th, 2730th, 2737th, 2744th, 2751th, 2758th, 2765th, 2772th, 2779th, 2786th, 2793th, 2800th, 2807th, 2814th, 2821th, 2828th, 2835th, 2842th, 2849th, 2856th, 2863th, 2870th, 2877th, 2884th, 2891th, 2898th, 2905th, 2912th, 2919th, 2926th, 2933th, 2940th, 2947th, 2954th, 2961th, 2968th, 2975th, 2982th, 2989th, 2996th, 3003th, 3010th, 3017th, 3024th, 3031th, 3038th, 3045th, 3052th, 3059th, 3066th, 3073th, 3080th, 3087th, 3094th, 3101th, 3108th, 3115th, 3122th, 3129th, 3136th, 3143th, 3150th, 3157th, 3164th, 3171th, 3178th, 3185th, 3192th, 3199th, 3206th, 3213th, 3220th, 3227th, 3234th, 3241th, 3248th, 3255th, 3262th, 3269th, 3276th, 3283th, 3290th, 3297th, 3304th, 3311th, 3318th, 3325th, 3332th, 3339th, 3346th, 3353th, 3360th, 3367th, 3374th, 3381th, 3388th, 3395th, 3402th, 3409th, 3416th, 3423th, 3430th, 3437th, 3444th, 3451th, 3458th, 3465th, 3472th, 3479th, 3486th, 3493th, 3500th, 3507th, 3514th, 3521th, 3528th, 3535th, 3542th, 3549th, 3556th, 3563th, 3570th, 3577th, 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5334th, 5341th, 5348th, 5355th, 5362th, 5369th, 5376th, 5383th, 5390th, 5397th, 5404th, 5411th, 5418th, 5425th, 5432th, 5439th, 5446th, 5453th, 5460th, 5467th, 5474th, 5481th, 5488th, 5495th, 5502th, 5509th, 5516th, 5523th, 5530th, 5537th, 5544th, 5551th, 5558th, 5565th, 5572th, 5579th, 5586th, 5593th, 5600th, 5607th, 5614th, 5621th, 5628th, 5635th, 5642th, 5649th, 5656th, 5663th, 5670th, 5677th, 5684th, 5691th, 5698th, 5705th, 5712th, 5719th, 5726th, 5733th, 5740th, 5747th, 5754th, 5761th, 5768th, 5775th, 5782th, 5789th, 5796th, 5803th, 5810th, 5817th, 5824th, 5831th, 5838th, 5845th, 5852th, 5859th, 5866th, 5873th, 5880th, 5887th, 5894th, 5901th, 5908th, 5915th, 5922th, 5929th, 5936th, 5943th, 5950th, 5957th, 5964th, 5971th, 5978th, 5985th, 5992th, 5999th, 6006th, 6013th, 6020th, 6027th, 6034th, 6041th, 6048th, 6055th, 6062th, 6069th, 6076th, 6083th, 6090th, 6097th, 6104th, 6111th, 6118th, 6125th, 6132th, 6139th, 6146th, 6153th, 6160th, 6167th, 6174th, 6181th, 6188th, 6195th, 6202th, 6209th, 6216th, 6223th, 6230th, 6237th, 6244th, 6251th, 6258th, 6265th, 6272th, 6279th, 6286th, 6293th, 6300th, 6307th, 6314th, 6321th, 6328th, 6335th, 6342th, 6349th, 6356th, 6363th, 6370th, 6377th, 6384th, 6391th, 6398th, 6405th, 6412th, 6419th, 6426th, 6433th, 6440th, 6447th, 6454th, 6461th, 6468th, 6475th, 6482th, 6489th, 6496th, 6503th, 6510th, 6517th, 6524th, 6531th, 6538th, 6545th, 6552th, 6559th, 6566th, 6573th, 6580th, 6587th, 6594th, 6601th, 6608th, 6615th, 6622th, 6629th, 6636th, 6643th, 6650th, 6657th, 6664th, 6671th, 6678th, 6685th, 6692th, 6699th, 6706th, 6713th, 6720th, 6727th, 6734th, 6741th, 6748th, 6755th, 6762th, 6769th, 6776th, 6783th, 6790th, 6797th, 6804th, 6811th, 6818th, 6825th, 6832th, 6839th, 6846th, 6853th, 6860th, 6867th, 6874th, 6881th, 6888th, 6895th, 6902th, 6909th, 6916th, 6923th, 6930th, 6937th, 6944th, 6951th, 6958th, 6965th, 6972th, 6979th, 6986th, 6993th, 7000th, 7007th, 7014th, 7021th, 7028th, 7035th, 7042th, 7049th, 7056th, 7063th, 7070th, 7077th, 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7959th, 7966th, 7973th, 7980th, 7987th, 7994th, 8001th, 8008th, 8015th, 8022th, 8029th, 8036th, 8043th, 8050th, 8057th, 8064th, 8071th, 8078th, 8085th, 8092th, 8099th, 8106th, 8113th, 8120th, 8127th, 8134th, 8141th, 8148th, 8155th, 8162th, 8169th, 8176th, 8183th, 8190th, 8197th, 8204th, 8211th, 8218th, 8225th, 8232th, 8239th, 8246th, 8253th, 8260th, 8267th, 8274th, 8281th, 8288th, 8295th, 8302th, 8309th, 8316th, 8323th, 8330th, 8337th, 8344th, 8351th, 8358th, 8365th, 8372th, 8379th, 8386th, 8393th, 8400th, 8407th, 8414th, 8421th, 8428th, 8435th, 8442th, 8449th, 8456th, 8463th, 8470th, 8477th, 8484th, 8491th, 8498th, 8505th, 8512th, 8519th, 8526th, 8533th, 8540th, 8547th, 8554th, 8561th, 8568th, 8575th, 8582th, 8589th, 8596th, 8603th, 8610th, 8617th, 8624th, 8631th, 8638th, 8645th, 8652th, 8659th, 8666th, 8673th, 8680th, 8687th, 8694th, 8701th, 8708th, 8715th, 8722th, 8729th, 8736th, 8743th, 8750th, 8757th, 8764th, 8771th, 8778th, 8785th, 8792th, 8799th, 8806th, 8813th, 8820th, 8827th, 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9709th, 9716th, 9723th, 9730th, 9737th, 9744th, 9751th, 9758th, 9765th, 9772th, 9779th, 9786th, 9793th, 9800th, 9807th, 9814th, 9821th, 9828th, 9835th, 9842th, 9849th, 9856th, 9863th, 9870th, 9877th, 9884th, 9891th, 9898th, 9905th, 9912th, 9919th, 9926th, 9933th, 9940th, 9947th, 9954th, 9961th, 9968th, 9975th, 9982th, 9989th, 9996th, 10003th, 10010th, 10017th, 10024th, 10031th, 10038th, 10045th, 10052th, 10059th, 10066th, 10073th, 10080th, 10087th, 10094th, 10101th, 10108th, 10115th, 10122th, 10129th, 10136th, 10143th, 10150th, 10157th, 10164th, 10171th, 10178th, 10185th, 10192th, 10199th, 10206th, 10213th, 10220th, 10227th, 10234th, 10241th, 10248th, 10255th, 10262th, 10269th, 10276th, 10283th, 10290th, 10297th, 10304th, 10311th, 10318th, 10325th, 10332th, 10339th, 10346th, 10353th, 10360th, 10367th, 10374th, 10381th, 10388th, 10395th, 10402th, 10409th, 10416th, 10423th, 10430th, 10437th, 10444th, 10451th, 10458th, 10465th, 10472th, 10479th, 10486th, 10493th, 10500th, 10507th, 10514th, 10521th, 10528th, 10535th, 10542th, 10549th, 10556th, 10563th, 10570th, 10577th, 10584th, 10591th, 10598th, 10605th, 10612th, 10619th, 10626th, 10633th, 10640th, 10647th, 10654th, 10661th, 10668th,

TABLE II—INCIDENCE OF SEPARATION AND DEGREE OF HISTOLOGICAL REACTION ASSOCIATED WITH VARIOUS TYPES OF NERVE SUTURE IN DOGS

Type of suture	No of operations	Number of operations in which separation of nerve ends was observed following suture*	Intensity of tissue reaction showing number in each group			
			+	++	+++	++++
Unmodified dog plasma† without clotting agent‡	16	5	8	4	2	
Unmodified dog plasma with rabbit clotting globulin	7	3	4	2	1	
Unmodified dog plasma with autologous muscle extract	5	1	2	2	1	
Heparinized dog plasma with rabbit clotting globulin	13	4	7	5		
Heparinized dog plasma with autologous muscle extract	3	0	2	1		
Whole blood	2	2		2		
Silk	11	0	8	3		
Nerve cut but not sutured	1	1	1			

\*Separation of nerve ends was observed at autopsy in each instance rather than immediately after suture at operation

†Homologous plasma was used in 2 instances in which the intensity of tissue reaction was 1 plus and 2 plus in the remaining experiments with clot suture, autologous plasma was used

‡2 animals in this group and 1 in which heparinized plasma with rabbit clotting globulin was used were not studied histologically

nitrate according to the Gros-Bielschowsky technique for impregnating axis cylinders. Segments of the nerve distal to the suture site were cut and Gros-Bielschowsky and Weigert-Pal preparations for the staining of axis cylinders and myelin sheaths were made.

Measurements of tensile strength of clots prepared from many samples of rabbit, dog, and human plasma were carried out. The values were obtained by an improvised method which proved simple and, in its final form, gave fairly consistent results (4). A detailed report of these studies will appear in a separate communication (1).

#### RESULTS

Of 41 instances in which all types of plasma clot suture were performed in rabbits, immediate and complete separation of the stumps to the extent of 1 millimeter or more occurred in 13, or almost one-third, of the total number (Table I). In 8 of these instances the separation exceeded 2 millimeters. There were 6 additional cases in which good apposition of nerve ends was present at the time of operation but in which subsequent examination of the suture site at autopsy revealed complete separation of the stumps. The total number of operations in which early or late separation occurred was 19, an incidence of about 46 per cent. The highest incidence of separation occurred in those cases in which suture was performed with the use of cockerel plasma clot. It should be noted that cockerel plasma clots differed strikingly from clots prepared from human, dog,

or rabbit plasma in being relatively nonretractile, inelastic, and friable.

In the operations on dogs separation of nerve stumps occurred in 13 of 44 instances, or 29.5 per cent of the attempted sutures which included a variety of types of plasma clot (Table II). Reduction in the incidence of separations was attributable to improvements in technique resulting largely from the use of the suturing mold.

The intensity of the tissue reaction at the suture site was evaluated after comparative study of histological sections of the nerve junction obtained at variable periods after operation. The reactions, ranging from 1 plus to 4 plus have been recorded in Tables I and II.

In the dog and rabbit the tissue reaction at the suture site was often very slight. In many instances the reaction was characterized by the appearance of a few connective tissue fibers and an occasional thin walled blood vessel, lymphocyte, monocytic cell, plasma cell, polymorphonuclear leucocyte, and fibroblast. Microscopic examination of the nerve several days after suturing with plasma clot revealed a small amount of granulation tissue at the suture site (Fig. 2), with homogeneous or granular eosinophilic material which represented the residual fibrin of the plasma clot. Lipophages were sometimes present in moderate numbers at this stage. Weeks later almost no signs of inflammatory reaction with the exception of a minimal increase of fibroblasts and connective tissue were observed at the nerve junction (Figs. 3, 4, and 5). In some instances in



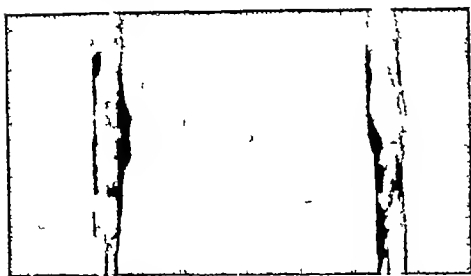


Fig 4. a, above, Photographs of a dog's sciatic nerves sutured with autologous unmodified plasma 35 days before specimens were obtained. Nerve on left was sutured with 11 drops of plasma mixed with 1 drop of rabbit clotting globulin, that on right with 8 drops of plasma and 1 drop of autologous muscle extract. b, Section through suture site of nerve shown on left in a. Suture site, indicated by arrow, is almost invisible. Hematoxylineosin stain  $\times 25$



Fig 4b

reaction subsided an increase of collagen and reticulum at the suture site became apparent

The tissue reactions of intermediate grade (++) and (+++) consisted of lesser focal accumulations of monocytic cells and lymphocytes (Fig 7a). At times polymorphonuclear cells with multinucleated giant cells, plasma cells, thin walled blood vessels, fibroblasts (Fig 8a), and connective tissue fibers were present in moderate numbers. These intermediate reactions usually occurred when heterologous plasma (human or cockerel) was used although occasionally they also followed the use of autologous plasma clot or silk suture (Fig 8a).

In general it may be stated that less cellular reaction occurred when autologous rather than heterologous plasma was used (Fig 9, a and b).

However, no appreciable differences in cellular response were found following autologous as contrasted with homologous plasma clot suture. At times less inflammatory changes followed suture with plasma clot than with silk but these differences were not consistent. It is uncertain also whether the use of different clotting agents such as mouse lung or rabbit muscle extracts or rabbit globulin caused any added tissue reaction above that resulting from the use of spontaneously clotted plasma.

In those instances in which whole blood was used as the suture material, granulation tissue composed of thin walled blood vessels with an

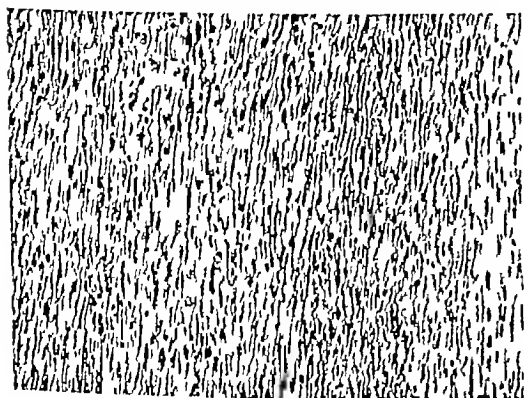


Fig 5 a, left, Higher power view of suture site shown in Figure 4, b. Note the almost complete absence of inflammatory or fibrotic reaction. Hematoxylineosin stain



$\times 133$  b, right, Axis cylinders at suture site which have grown through the junction. Impregnation with silver nitrate, Gros Bielschowsky method.  $\times 118$

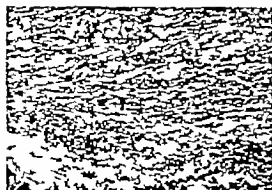


Fig. 6a



Fig. 6b

occasional lymphocyte plasma cell, monocytic cell, and polymorphonuclear leucocyte was present. Great numbers of pigment laden macrophages were found in these cases and after the lapse of weeks, fibrosis was rather prominent. Separation of the nerve stumps occurred in the few instances in which suture with blood was attempted.

The degree of adhesions which was found grossly between the suture site and the surrounding tissue closely paralleled the intensity of the inflammatory and fibrotic tissue reaction observed microscopically. Only few delicate adhesions were seen when minimal histological reaction was present. Trauma to the muscle or other tissue adjacent to the nerve as well as hemorrhage during the operation tended to increase adhesions.

Fig. 6. a, left, Focus of round cells 45 hours after suture with 11th cockerel plasma and chick embryo extract. b, above, Diffuse cellular infiltration 3 days after suture with 11th cockerel plasma (about clotting agent)  $\times 33$ .

Nerve fibers readily grew through the plasma clot junction (Fig. 5b). In Figure 9c unstimulated nerve fibers are seen 10 centimeters distal to the suture site. There is at present no indication from these studies that the regeneration of axon cylinders occurs less rapidly after plasma clot than after silk suture. Histological study of the pattern of regenerating nerve fibers following different suturing procedures indicated that no distortion of nerve fibers occurred when plasma clot suture was carried out with the aid of the mold. In contrast with this one may note the greater disorganization of nerve pattern resulting from the use of silk sutures (Fig. 3a).

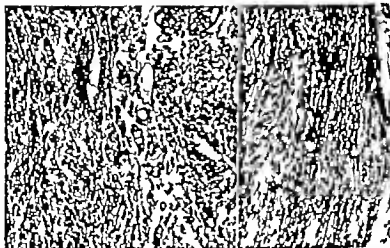


Fig. 7. a, left, Focus of round cell infiltration 97 days after suture with human unmodified plasma. b, right, Minimal histological reaction 59 days after suture with human plasma.  $\times 35$ .



Fig 8 Photomicrographs showing tissue reaction 28 days, a, left, and 48 days, b, right, after silk suture. Note the foreign body giant cells in a and the connective tissue encapsulation of the silk in b.  $\times 1285$

#### EVALUATION

In order to qualify as desirable nerve suture material, plasma clots must not provoke excessive inflammatory or fibrotic reaction of tissues. They must, moreover, possess sufficient strength to

maintain nerve ends in good apposition until union by fibroblasts or Schwann cells occurs. Clots formed from 7 to 15 drops of autologous or homologous plasma appear usually to fulfill the first requirement. Under the conditions of the

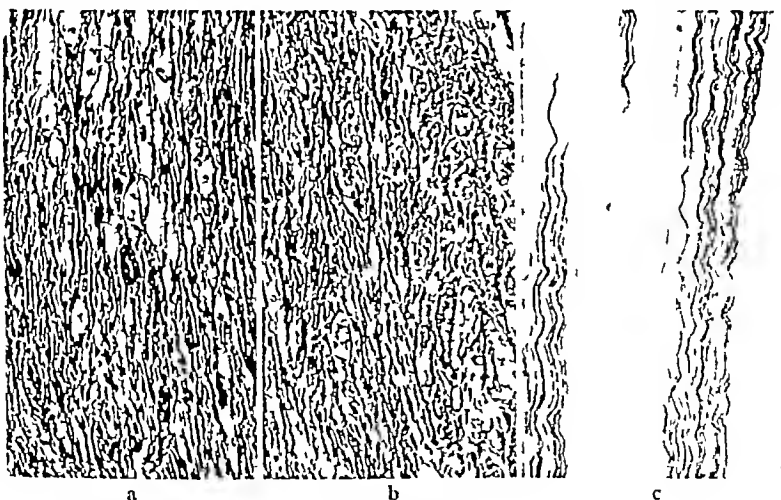


Fig 9 Photomicrographs showing minimal histological reactions at suture site, a, 20 days after autologous unmodified plasma and b, 50 days after autologous heparinized plasma clot suture.  $\times 136$ . In c, nerve fibers are shown stained by Weigert-Pal technique in portion of nerve 10 centimeters distal to suture site, specimen obtained 95 days after autologous unmodified plasma clot suture.  $\times 68$ . All sections seen in Figures 6, 7, 8 and 9 (except Fig 9c which is stained by the Weigert-Pal technique) represent suture sites on sciatic nerves of rabbits stained with hematoxylin-eosin.



experiments as carried out in the present study the clots failed to meet the second requirement in a high proportion of instances. However it must be remembered that no form of immobilization of the limbs was attempted following operation. In more recent experiments, following plasma clot suture of the sciatic nerve, the hind limbs have been immobilized by means of plaster-of-paris casts in such a position as to remove tension from the suture site. Conditions are thus rendered more favorable for plasma clot suture. When tension exists at the suture site plasma clot suture is contraindicated since the risk of separation of nerve stumps is too great.

It must be emphasized that trauma to the nerve ends during their manipulation as well as injury to muscle or other tissues around the nerve or hemorrhage in the region of the suture site all tend to aggravate the inflammatory response of the tissues. Misinterpretations may thus arise as to the amount of reaction attributable to the presence of the plasma clot. It is probable that the histological reaction observed in association with some of the various types of suture material, especially in our earlier operations in rabbits was due in part to such trauma or hemorrhage. However special care was taken to avoid such pitfalls in later operations and it seems fair to conclude that the different histological reactions which occurred following the use of various suture materials resulted principally from the substances mentioned.

The greater intensity of the inflammatory reaction around nerve junctions sutured with cockerel plasma as compared with those in which human plasma was used is apparently at least in part, attributable to the fact that fortified cockerel plasma was used. In the one case in which unfortified cockerel plasma was used, minimal amount of reaction occurred. It is possible too that the chick embryo extract played a role in this greater inflammatory response. That this extract is not the most important factor however is indicated by the intense inflammatory reaction which occurred in the instances of cockerel plasma clot suture in which no thymic extract was used.

It is as yet uncertain whether autologous plasma and clotting agents cause less tissue reaction than homologous ones. The observation that less inflammatory change generally followed the use of autologous rather than heterologous plasma is in keeping with the results of Loeb's investigations of blood clots.

It seems clear that the use of the mold casts for a more satisfactory nerve suture. Its advantages lie in the fact that it enables one to secure more perfect alignment of the nerve stumps, it minimizes trauma to the nerve from excessive manipulation and it permits the clots to surround the nerve junction more completely thereby increasing the strength of the union.

#### CONCLUSIONS

1. Cockerel or human plasma clot suture of nerves in rabbits generally result in more inflammatory and fibrotic reaction than does silk suture.
2. Autologous plasma clot suture of nerves in rabbits and dogs usually results in very little inflammatory or fibrotic change and compares favorably in this respect with silk suture.
3. Separation at the suture site frequently follows plasma clot suture in rabbits when small quantities of plasma are used. The incidence of separation was appreciably reduced in operations on dogs by the use of a special rubber mold which retains the plasma uniformly around the wound site during the clotting process.
4. Nerve fibers readily grow through the junction formed by means of plasma clots.
5. Plasma clot suture offers promise as a method of securing junction of nerve ends with minimal distortion of nerve pattern in instances in which the factor of tension at the suture site can be eliminated.

#### REFERENCES

- GOLDWARR, A. I., TARLOW, I. M., BOYCE, E. and SMITH, A. S. To be published.  
 LOEB, L. Arch. Path. 930, 224  
 3. TARLOW, I. M. and BEYONCE, B. Science, 1937, 75, 57.  
 4. TARLOW, I. M., GOLDWARR, A. I. and BEYONCE, B. J. Lab. Clin. 31, 31, 37, 333.  
 5. VOTAW, J. Z., and MILLER, W. P. B. Lancet, Lond. 940, 36.

# EDITORIALS

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## SURGERY Gynecology and Obstetrics

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MARCH, 1943

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### CANCER OF THE STOMACH

WHILE remarkable results are being obtained in the treatment of cancer of the colon and rectum, cancer of the stomach is far less often cured, and the consequence is that most laymen and many physicians look upon it as a rather hopeless disease. Some of this pessimistic attitude seems to be justified, for even the best reports of treatment of gastric cancer do not compare favorably with those of cancer elsewhere in the body. Since this is so, it behooves the physician and surgeon to try to improve their results. How may this best be done, and what is being done about it?

With improvements in preoperative preparation, technique, equipment, anesthetic methods, and postoperative care, surgeons have greatly widened the field of operability and the extent of operative removal in cases of cancer of the stomach. Total removal of the stomach, which was regarded as a rarity only a few short years ago, is now a more or less standard procedure, and every large clinic in

which much gastric surgery is done has its own series of total gastrectomies. While the results of total gastrectomy have not been too brilliant, the aggregate of patients who have lived for one to several years after such an extensive procedure in reasonably comfortable condition must be considerable. For example, from the Massachusetts General Hospital alone in 1938, Arthur Allen<sup>1</sup> reported 16 cases of total gastrectomy, 8 of which "left the hospital in a comfortable state of health." In addition, in nearly every large clinic, surgeons have increased the number of patients operated upon by enlarging their criteria of operability. For example, at the Cincinnati General Hospital in the years 1932-1936 inclusive, 42 per cent of the patients in whom cancer of the stomach was diagnosed were operated upon, the others being deemed inoperable, and in only 9 per cent of these were resections done. In the years 1937-1939 inclusive, 50 per cent of the patients with gastric cancer were operated upon, and in 43 per cent of these resections were done. The same sort of experience has been noted in other hospitals.

The increase in percentage of operable cases is in part due to earlier diagnosis and treatment, but in even greater part to a willingness on the part of surgeons to perform resections in patients who previously would have been regarded as inoperable. One cannot, of course, expect excellent end-results when many borderline cases are treated by resection, but often some months or years of reasonably comfortable life are given to patients who otherwise have a miserable outlook. With increases in the operability, the surgeon has added wider extent of resection to the cases which he regards

<sup>1</sup>Am J Surg 1938 39 35

# MEMOIRS

GEORGE CRILE

1864-1943

ONE of the most remarkable careers in the history of American surgery came to a close in the death of Dr. George Crile at the Cleveland Clinic Hospital on January 7, 1943. The fatal illness was due to subacute bacterial endocarditis and *Streptococcus faecalis septicemia*.

Dr. Crile was born in Chili, Ohio, November 11, 1864, the son of Michael and Martha Deeds Crile. He graduated from Ohio Northern University and from Wooster Medical School, now Western Reserve University, in 1887. During the next two years he studied in Vienna, Paris, and London, and upon his return became lecturer and demonstrator in histology and subsequently professor of principles and practice of surgery at Wooster University. He was professor of surgery at Western Reserve University and surgeon to the Lakeside Hospital from 1911 to 1924. In 1921 he and his associates established the Cleveland Clinic and in 1924 completed the Cleveland Clinic Hospital.

Dr. Crile's life was one of amazing energy which he maintained up to the time of his final illness. It was not surprising that a man of such personality of such initiative, driving power, and independence of thought should have become known throughout the entire surgical world. His capacity for making friends, his infectious enthusiasm, his optimism, and his unfailing courtesy to his assistants and his staff made visitors to his clinic as welcome as he himself was wherever he traveled. His diversity of interests and accomplishments provides unlimited material for a biographical sketch, but it is only possible to refer briefly to those activities which will be accepted as representing at least some of his noteworthy achievements.

As a surgeon, Dr. Crile's reputation was based on unusual professional attainments and personal attributes. He was a master craftsman and exponent of the art of surgery. It was this superlative technical skill and all that it implied which led to his investigations as to the causes of surgical shock and the means of its prevention. The theory and practice of anoxi-association were the result. Surgeons accepted this in principle but they were also aware that the primary factor in reducing surgical trauma to a minimum was the consummate skill with which he carried out every operation. In this one respect alone, Dr. Crile contributed immeasurably to the advancement of surgery in this country, as did the late Lord Moynihan in the same way in Great Britain.

Conspicuous in Dr Crile's achievements in surgery was his pioneer work in the surgery of the endocrine system, particularly in the surgical treatment of diseases of the thyroid and parathyroid glands. In this field, his experience was enormous. His inquiring mind found ample scope in the physiology of the endocrine system and his efforts to connect disorders of this system with other diseases and to attempt to control them by surgical procedures have been one of the most stimulating chapters in medicine. It was this curious desire to explore the unknown together with his great surgical skill which made Dr Crile such a unique figure in the surgical profession.

The writings of Dr Crile are an accurate measure of his range of activities and interests. His early papers were concerned chiefly with results of his surgical experience and, as were other clinical surgeons of his day, he was constantly searching for safer techniques. The operative procedures which he developed and the clarity with which he described them had much to do with the development of surgery during his lifetime. The more important contributions were his method of direct blood transfusion, the technique of thyroidectomy, laryngectomy, the removal of esophageal diverticulum, biliary operations, and the operative procedures on the gastrointestinal tract. As the sequence of his publications is followed, one will find evidence of the theory that the human organism is an electrochemical mechanism and his studies of the interrelation of the thyroid gland, the suprarenal glands, and nervous system from both a clinical and experimental standpoint became the basis for an approach to the problems of hyperthyroidism, peptic ulcer, and essential hypertension. With all this activity in research, he continued to contribute authoritatively the results of his vast experience in surgery of the thyroid gland, in the surgical management of cancer in various situations, and in diseases of the gall bladder. Throughout all his writings, one will find a constant effort to reduce mortality and morbidity of operations, and it was in the application of these principles that he contributed so greatly to his own fame and to the prestige of American surgery.

The development, in 1921, of the Cleveland Clinic and Foundation is a story of a group of men who throughout all their professional lives had been associated in medical practice and thus developed a rapidly growing nucleus of organization. These men were the late Dr F E Bunts, Dr Crile, and Dr William E Lower, all of whom had been engaged in teaching in the medical school in Wooster University and in Western Reserve University and who had been colleagues in the organization of the Base Hospital of Lakeside Hospital which was attached to the American Expeditionary Force in the first World War. When this unit returned to the United States in 1919, the Cleveland Clinic was organized and has provided such splendid facilities for sound clinical practice, research, and education of graduate students as to bring world reknown to Dr Crile and his associates.

No greater evidence can be found of Dr Crile's amazing vitality than his ability with all the responsibility of organizing the Clinic and Foundation, to give his time and interest to so many professional societies and associations. He was particularly active in the American Surgical Association of which he was president in 1923 in the Southern Surgical Association and in the Association for the Study of Colter. He was a member of the editorial board of *SURGERY GYNECOLOGY AND OBSTETRICS*, from 1920 to 1942 and also held similar offices in other scientific journals.

Dr Crile was one of twelve men who in 1912 formed a committee for the organization of the American College of Surgeons. He became a member and eventually chairman of the first Board of Regents, a position he held until his resignation in October 1939, when he passed on the chairmanship to Dr Irvin Abell. Dr Crile was president of the College in 1916-17 and upon his resignation as a regent in 1941 he was appointed to the Advisory Council. At the death of Dr Franklin Martin who had been Director General of the College until 1935 Dr Crile gave liberally of his time and support to the work of the College, particularly in respect to such activities as hospital standardization, clinical research, and publications. He saw as did others, that there was needed in this country a society of surgeons more inclusive than those societies of limited membership and that such an association could do much to give more skilled surgical care to the American people. The approach to this was sound as it was based on according fellowship in the College to those surgeons who eight years or more after graduation from medical school had demonstrated to their colleagues and to the State Committees of the College that they were competent surgeons. The purposes and ideals of the College in which Dr Crile so sincerely believed were well expressed by Dr Crile himself in the Annual Oration on Surgery at the San Francisco Clinical Congress in 1935.

It should be borne in mind that we are building not in the interest of the profession but primarily in the interest of the people at large. The automobile, the airplane and other methods of transportation the machinery of civilized man is so distributed on the farms and ranches, in the mines, on the highways, on railways and in the air that everybody is on the front line so that in the case of an accident, disease or a surgical operation it is a necessary to have a good surgeon in the most remote place. It is not true that we have one in San Francisco, Los Angeles, Boston, New York, or Philadelphia. Therefore our task is to see to it that there are good surgeons all over Canada and the United States and wherever there is human being who requires the service of a surgeon there must be a good surgeon and a good hospital.

An example of Dr Crile's broad experience in surgical organizations is the fact that he was a charter member in the Society of Clinical Surgery which was organized in 1903 and the first meeting was held in Baltimore. The meetings also included visits to clinics in Great Britain and the continent. At the last Cleveland meeting in 1936 the members will I am sure never forget the drama of seeing Dr Crile at the age of seventy-two years, perform celiac ganglionectomy for hypertensive disease.

Dr Crile was an important factor in making the Interstate Postgraduate Association of North America the outstanding course of postgraduate instruction in the world. This association has set such a splendid example of what can be accomplished that several similar organizations have been formed. Dr Crile's part in the development of the Interstate Postgraduate Association was recognized by the presentation of a medal at special ceremonies in 1937.

Dr Crile's war record is as conspicuous as any of his varied activities. He served during the Spanish-American war as a Brigade-Surgeon in the Porto Rican Campaign. He was one of the first group of physicians appointed to the Medical Reserve Corps and served as special professor at the Army Medical School, Washington, D. C., during 1913-14. During the first World War, Dr Crile, in his civilian capacity, served as surgical director of the American Ambulance Hospital (The Lakeside Unit) in France and returned to the United States to become director in charge of the staff of Base Hospital No. 4, which was organized under the auspices of the Lakeside Hospital. This was the first unit of the United States Army to reach Europe, and it remained with the British Expeditionary Forces in France during its entire overseas existence and operated as No. 9 General Hospital. When this unit was demobilized in 1919, Major Crile was assigned as senior consultant in surgical research and as clinical director. At the close of the World War, he was appointed Colonel in the Medical Reserve Corps and was also cited for distinguished service by the British government in a dispatch from Field Marshal Sir Douglas Haig. He was appointed Brigadier General in the Medical Reserve Corps in 1921 and was awarded the Distinguished Service Medal and in awarding this medal, the Commanding General said of Dr Crile: "By his skill, researches and discoveries, he saved the lives of many of our wounded soldiers. His tireless efforts to devise new methods of treatment to prevent infection and surgical shock revolutionized Army surgery and met with the greatest success." In the present war, Dr Crile was made honorary consultant to the Medical Department of the United States Navy.

Dr Crile's pre-eminence in the surgical world is evidenced by the honorary degrees, citations and awards he received from the highest educational institutions. As he advanced in years Dr Crile began to devote more of his time to recreation and travel, and even in these later activities his interest in scientific medicine and research continued. It was during these travels that Dr Crile collected great numbers of sea and land animals from all parts of the world and observed the differences in power and personality of these animals in relation to the comparative sizes of the brain, thyroid gland, suprarenal glands, and sympathetic nervous system. In 1935, he donated to the American College of Surgeons an extensive exhibit of many of his specimens which duplicated one in Cleveland. In the winter of 1923-24, he organized and conducted an ornithological expedition to the tip of southern Florida and in 1935, with Mrs Crile, he made a trip

to Africa to make a study of wild life. The fascinating story of this trip is told in a book written by Mrs. Crile entitled *Skyscrapers to a Jungle Laboratory: an African Adventure*.

The passing of Dr. Crile will be mourned by his colleagues, his associates, and his assistants and the surgical profession of the world will pay tribute to the influence of a superb surgeon, a great organizer, an indefatigable and original worker and a buoyant and stimulating personality.

DOUGLAS C. BALFOUR

# CRILE, GEORGE

Born in Chilli, Ohio, November 11, 1864; son of Michael and Margaret (Dieta) Crile. Died, Cleveland, January 7, 1943.

Married Grace McBride of Cleveland, February 7, 1900.

Children: Margaret (Mrs. Hiram Garretson), Elizabeth (Mrs. J. A. Criler, Jr.), George Jr., Robert.

Ohio Northern University A.B. 1884, A.M. 1888.

Wooster University (Western Reserve University) M.D. 1887, A.M. 1894, LL.D. 1916.

Postgraduate study in Vienna, 1893; London, 1895; Paris, 1897.

Honorary degrees: Hiram College, Ph.D., 1901; University of Dublin, M.Ch., 1903.

University of Glasgow, LL.D., 1908; University of Guatemala, Doctor honoris causa, 1939.

Lecturer and Demonstrator of Histology, 1889, 1890; Professor of Physiology, 1890-1893; Professor Principles and Practice of Surgery, 1893-1900; Wooster University.

Professor of Clinical Surgery, 1900-1911; Professor of Surgery, 1911-1924; Emeritus.

Professor of Surgery, 1924-1943; Western Reserve University.

Visiting Surgeon, Lakeside Hospital, 1911-1924.

Founder and director, Cleveland Clinic Foundation, 1911-1943.

Surgeon, Cleveland Clinic Hospital, 1924-1943.

Member of Editorial Board, *SURGERY GYNECOLOGY AND OBSTETRICS*, 1920-1942; member Board of Directors, Surgical Publishing Company of Chicago, 1935-1942.

Brigade Surgeon of Volunteers, Major, Cuba and Puerto Rico campaign, 1898; Major.

Med. O.R.C. and director, U.S.A. Base Hospital No. 4, Lakeside Unit (B.E.F.).

N. 9) in France, May 1917-May 1918; Senior Consultant in Surgical Research,

May 1918-January 1919; Lieutenant Colonel, M.C. June 1918; Colonel, November

1918; Brigadier General, Med. O.R.C., 1921.

Awarded Distinguished Service Medal (U.S.) 1919; honorary member Military Division

3d class, Companion of Bath (British), 1919; Chevalier Legion of Honor (French),

1919; Alvarenga prize, College of Physicians, Philadelphia, 1901; Cartwright prize,

Columbia University, 1897 and 1903; Senior prize, American Medical Association,

1898; American medal for service to humanity, 1914; National Institute Social

Sciences medal, 1917; Trimble lecture medal, 1921; 3d Laureate of Lannelongue

Foundation medal, Société Internationale de Chirurgie de Paris, 1925; Cleveland

medal for public service, 1931.

Memberships in medical and other organizations: American Association Anatomists,

American Association for the Advancement of Science, American Surgical Association,

—president, 1913; American College of Surgeons—president, 1916; member organ-

izing committee, Regent, Chairman, Board of Regents, member Advisory Council,

Board of Regents, 1914-1943; 2nd member of Cancer Committee, Committee on

Hall of Art and Science, Committee on Inter-American Relations, Medical Mission

Pictures, Co operating Committee with American College of Physicians, American Medical Association, American Physiological Society, American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Southern Surgical Association, Southern Medical Association, American Philosophical Society, Association American Pathologists and Bacteriologists, Society of Clinical Surgery, Society of Experimental Biology and Medicine, National Institute of Social Sciences, National Research Council, Association for the Study of Internal Secretions, American Heart Association, American Medical Editors' Association, Ohio State Medical Association, Cleveland Academy of Medicine, Cleveland Medical Library Association, American Association for the Study of Goiter, American Board of Surgery, Founders Group, Interstate Postgraduate Medical Association of North America, Union Club of Cleveland, and of various American and European societies

*Books* Surgical Shock, 1897, Surgery of the Respiratory System 1899, Certain Problems Relating to Surgical Operations, 1901, On the Blood Pressure in Surgery, 1903, Hemorrhage and Transfusion, 1909, Anemia and Resuscitation, 1914, Anoci-Association (with Lower), 1914, 2d ed title, Surgical Shock and the Shockless Operation through Anoci-Association, 1920, Origin and Nature of the Emotions, 1915, A Mechanistic View of War and Peace, 1915, Man, An Adaptive Mechanism, 1916, The Kinetic Drive, 1916, The Fallacy of the German State Philosophy, 1918, A Physical Interpretation of Shock Exhaustion and Restoration, 1921, The Thyroid Gland (with others), 1922, Notes on Military Surgery, 1924, A Bipolar Theory of Living Processes, 1925, Problems in Surgery, 1928, Diagnosis and Treatment of Diseases of the Thyroid Gland (with others), 1932, Diseases Peculiar to Civilized Man, 1934, The Phenomena of Life, 1936, The Surgical Treatment of Hypertension, 1938



# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

A SUMMARY is presented in *Nutrition and Chemical Growth in Childhood* by Icie G. Macy Ph.D. of the research work in biochemistry of childhood carried out by the Children's Fund of Michigan under the directorship of the author. Volume I *Evaluation* is a book of 38 pages. Volume II *Interpretation* has not yet been published.

The present volume is very well arranged giving many of the laboratory results of the author's experiments. It is profusely illustrated. The last third of the book is taken up almost exclusively with laboratory methods and the treatment of scientific data. The book is not in any sense a summary of the world's literature on the subject, being rather a conscientious report of the author's experiments. It can, therefore, be recommended as a source book of information on the extensive studies made by the Children's Fund of Michigan. For those interested in laboratory methods and research on this subject it provides excellent material. The second volume, not yet published, which Dr. Macy will discuss the interpretation of her findings should be of wider interest to the general reader.

C. ANDERSON MORRIS.

A TREATISE on the art of looking at the surgical patient with acumen is presented in *Diagnoses of Physical Signs in Clinical Surgery* by Hamilton Bailey M.A. Many signs of disease and methods of examination overlooked by the inexperienced or careless surgeon are illustrated by pertinent text and excellent illustrations, both of which reflect a sound knowledge of the underlying pathological condition and the relative importance of physical diagnostic methods.

Mr. Bailey's book is worthy successor to De Quervain's *Surgical Diagnosis* which for many years has been a classic in this field.

While briefly speaking there is no bibliography given, every illustrative feature contrasts referring footnotes to the names of medical men whose names are associated with clinical signs, complexes, or methods of examination, often giving their birth

*Illustrations of Physical Signs in Clinical Surgery* by Hamilton Bailey F.R.C.S. Long, 49, Abchurch Lane, London E.C. 4, 1941.

*Illustrations of Physical Signs in Clinical Surgery* by Hamilton Bailey F.R.C.S. Long, 49, Abchurch Lane, London E.C. 4, 1941.

dates, places of residence and positions held by each.

Particularly valuable chapters are devoted to the diagnosis and pectoral characteristics of myelomata of the neck, salivary glands, and thyroid. The chapter on lesions of the male genitalia reflects particular interest and skill on the part of the author in this particular field.

The whole book is excellently edited and printed and is pleasant to read.

The author holds most properly that the correct appraisal of physical methods of examination coupled with the detection of local signs of disease will precede special laboratory methods or surgical exploration in diagnosis. It has successfully selected, described, and depicted these methods and signs which with intelligent use add the Sherlock Holmes touch to surgical diagnosis.

Victor Dunn.

TO cover the broad field of infections, injuries, fractures, repair of nerves and tendons, congenital deformities, tumors and diseases of the hand in a single volume is an ambitious task, and Crisp has accomplished it very well in his *The Hand: Its Disinfection and Disease*.

The section on specific and chronic infections of the hand (Chapter III) is particularly well done and well illustrated. The chapter on burns is disappointing in that it does not outline the various local methods of treatment and bring out in clear fashion the importance of securing a clean growing surface at the earliest possible moment and covering areas of whole thickness loss with grafts of intermediate thickness.

The section on incised and lacerated wounds is done. One would wish more emphasis had been laid on the importance of a bloodless field and of hemostasis which a cold cutting across flexion creates. (The same comment might be made concerning the discussion of the care of infections.)

Chapters on fractures, dislocations, repair of reconstruction and tumors are well written and well illustrated. All in all the author has drawn on his own extensive experience and on that of others to produce a very readable and helpful contribution to the subject of hand surgery.

JOHN L. KERR.

*The Hand: Its Disinfection and Disease* by Crisp, J. W. D. P. A.C.S. Philadelphia and London W. B. Saunders Co. 1941.

# SURGERY

## GYNECOLOGY AND OBSTETRICS

*An International Magazine, Published Monthly*

VOLUME 76

APRIL, 1943

NUMBER 4

### DELAYED CLOSURE OF INCISIONS MADE AT CLOSURE OF COLONIC STOMAS

JOHN deJ PEMBERTON, M D, F A C S, and B MARDEN BLACK, M D,  
Rochester, Minnesota

**F**ORMERLY it was our custom to manage the incision remaining in the wall of the body after closure of a colonic stoma in essentially the same manner as that in which other incisions of the abdominal parietes are treated. After the opening in the bowel had been closed, the fascia was approximated above the bowel, and the subcutaneous layer and skin were closed snugly. A Penrose drain was so placed that it extended down to the suture line in the bowel. For the most part, such wounds healed satisfactorily, but occasionally rather extensive indolent, subcutaneous abscesses developed. This was true particularly when fecal drainage occurred, in such cases the fecal fistula sometimes failed to close, and subsequent attempts at operative closure were necessary. Infections commonly occur in incisions made for closure, since some degree of contamination by the contents of the bowel at the time of the closure cannot be avoided and since secondary incisions made within a few months thereafter through the scar of a previous incision are less resistant to infection than are primary incisions. Furthermore when fecal drainage occurs, there is extensive and persistent contamination and such drainage is not unusual.

#### ANTECEDENT INVESTIGATIONS

About 2 years ago, in an attempt to better our results, particularly in respect to the development of subcutaneous abscesses and fecal fistulas, we adopted the method of delayed closure recently advocated by Collier and Valk for the management of contaminated incisions. These authors reported that the method, known at that time as "delayed primary suture," was first employed extensively and its worth proved by French surgeons in 1918. It was found to be so well suited to military needs, and the results which followed its use were so superior to those which followed primary suture of contaminated war wounds, that it was soon adopted by surgeons in the British and American forces. Since the time of the war of 1914-1918, this method has been widely used for the management of contaminated lacerations (3).

The terms "delayed closure" and "delayed primary suture" mean essentially that the incision is packed open for a time before being closed. Pool thought that the distinction between "delayed primary suture" and "delayed secondary suture" was a matter of tissue rather than of time. A "delayed primary" is one in which the edges can be approximated and will unite without the use of sutures, whereas secondary suture is one in which the epidermis has grown inward.

From the Division of Surgery of the Mayo Clinic, Rochester, Minnesota.

cised for proper union. The distinction, according to Hepburn, was based on the appearance of granulations in the wound, and the time for delayed primary suture usually was considered to be any time before the appearance in the wound of granulations visible to the naked eye. Hepburn proposed however that the term be restricted to use in those cases in which suture is undertaken at the time the original packing is removed. The best results were found to follow those closures done within 50 hours after the original operation.

It is not entirely clear why delay of closure of a contaminated incision should result in fewer infected incisions. At the time the method was first used it was assumed that heavily contaminated wounds were not suitable for suture as a result after débridement smears and cultures were made and the wounds were packed open pending receipt of reports from these examinations. If a large number of organisms of any type were present or if hemolytic streptococci were present the incisions were not considered to be suitable for suture and were treated by some other method. As experience increased however it became evident that knowledge of the type or types of organisms present in the wound as judged by the results of smear and culture could not be relied on as a basis for prediction as to the success or failure of the delayed suture. Meanwhile it had become apparent that incisions which had been packed open did far better than those that had been sutured primarily. Collier and Valk cultured material obtained from ten wounds contaminated by discharges from the lower bowel. In each case there was a preponderance of the *Escherichia coli* with fewer of the *Staphylococcus aureus* and anhemolytic streptococci. Material from the same wounds was cultured again after the wounds had been packed open for 24 hours. Result of culture was in all cases positive and the types of organisms found remained the same. Collier and Valk concluded that such a method of packing did not have a bactericidal effect.

Such evidence suggests that packing of a wound open for a period before closure is effective leads to certain changes in the wound which in turn produce an environment less favorable for the persistence of organisms known

to be present. On the basis of our own observations, we believe that packing of a wound open for a period, until the surfaces of the wound are relatively dry prevents to a large extent the collection of serum or blood in the wound. Such collections in already contaminated wounds will almost certainly lead to infection of the wound. In this connection, we may say that Hepburn noted that war wounds that had been packed open in anticipation of delayed primary suture did poorly if a blood clot had collected beneath the pack. Apart from this, the usual explanation (1, 2, 6) for the better results which follow delayed closure is that after coagulation has occurred on the fresh surface of the wound, the open mouths of sectioned lymphatic and blood vessels are plugged and rapid absorption of bacteria cannot occur. Du Mortier was able to demonstrate experimentally that with the passage of time sutured incisions became increasingly resistant to infection and that when infections did occur they were less extensive. He made incisions through the skin, subcutaneous tissue and muscular layer of the abdominal wall of guinea pigs and swabbed gently after varying intervals of time. The sutured incisions with a fresh virulent culture of what he called the "*Staphylococcus aureus hemolyticus*." He found that there was a well defined period of about 6 hours during which resistance of the tissue to bacterial invasion was minimal. During this period the bacteria caused not only local suppuration but also invaded the surrounding tissues and initiated spreading infections. When on the other hand, the bacteria were swabbed on the sutured incisions 12 hours after operations, most of the incisions became infected but the infections remained localized. From this time (that is, 12 hours) onward, the percentage and severity of infections steadily decreased until 5 days after operation, it was no longer possible to infect the wounds by swabbing on the cultures.

The optimal interval at which the wound should be packed open is not known with certainty. On the basis of experience in the treatment of war wounds, the best results for closure carried out within 50 hours of the operation. Collier and Valk believed that there is little to be gained by delay of closure for more

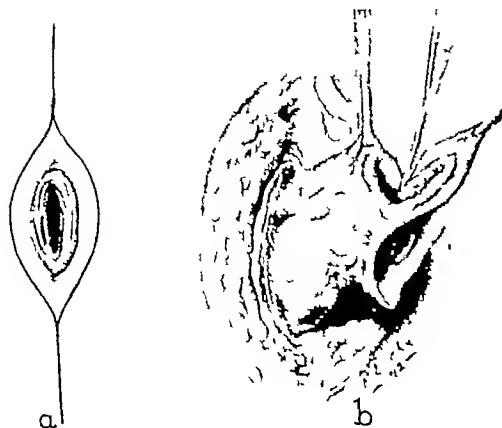


Fig 1

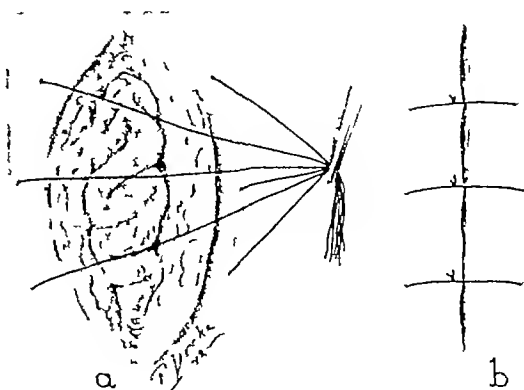


Fig 3

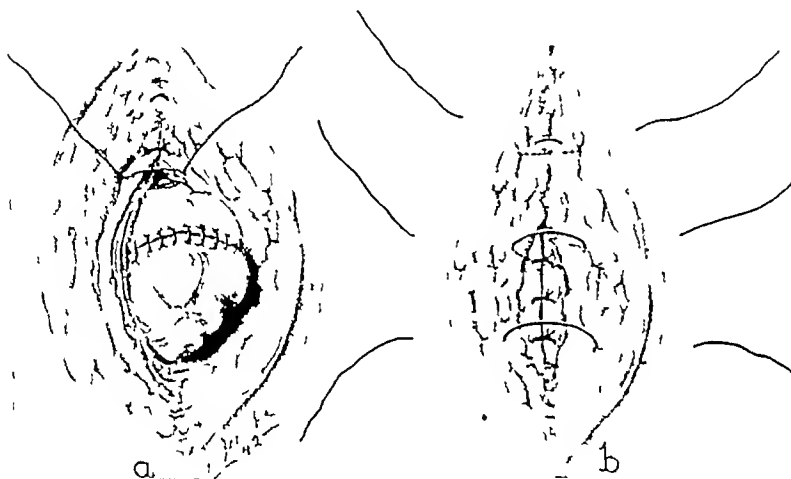


Fig 2

Fig 1 a, Incision made in the skin through the scar of the original incision made in performance of colostomy the incision is carried around the opening in the bowel, so that a small margin of skin remains, b, technique of dissection of bowel from the body wall. The cuff of scar tissue and skin around the opening in the colon is partially excised.

Fig 2 a, The opening in the colon is closed, and the fascial layer is partially closed, complete closure of this

layer above the bowel restores the strength of the body wall, b, the fascia is closed completely above the bowel, silkworm gut sutures are in place.

Fig 3 a, The iodoform gauze pack is in place, holding the skin and subcutaneous tissues open, and the ends of the silkworm gut sutures are held in a hemostat, b, appearance of final closure after the pack has been removed and the silkworm gut sutures have been tied.

than 24 hours. We have waited 48 hours, however, before closure of incisions in the belief that after such an interval the patient will have had time to recover somewhat from the operation and that surfaces of the wound appear drier at end of 48 hours than at end of 24

#### TECHNIQUE

The technique of our present method of closure of colonic stomas differs from our former

method of closure only in the treatment of the skin and subcutaneous tissues. It should be emphasized that before closure is attempted there must be adequate room to permit the bowel to be closed without encroaching on its lumen, and that the spur must have been adequately destroyed. An incision which is sufficiently long to provide adequate exposure is made through the scar of the former incision and is carried around the opening in the bowel

TABLE I. — COMPARISON RESULTS AFTER DELAYED AND PRIMARY CLOSURE OF EXCISIONS MADE AT CLOSURE OF COLONIC STOMAS

Cases	Type of closure	
	Primary	Delayed
Without fecal drainage	29	33
With fecal drainage (spontaneous)	7	7
With fecal drainage (closure around clamp)		7
Total	47	47
Closure failed	7*	1

\*One failure due possibly to inadequately destroyed spur

†One closure to inadequately destroyed spur

The bowel is freed up from the body wall and the fascia is cleaned of fat and scar tissue sufficiently to provide a definite layer which subsequently can be approximated to restore the strength of the body wall. Generally this can be done without making an opening into the peritoneal cavity but if a small opening is made inadvertently through the peritoneum little harm will be done since it can be closed promptly before opportunity for soiling arises. The skin and scar tissue around the opening in the bowel are excised (Fig. 1 a and b). The opening in the bowel is closed transversely to the long axis of the bowel with two rows of continuous surgical gut sutures (Fig. 2 a and b). The previously freed up muscular and fascial layer is approximated above the sutured bowel with interrupted surgical gut sutures. Silkworm gut sutures are then placed as is shown in Figure 2 b. A generous "bite" is taken through the skin on one edge of the wound; the needle is reversed to pick up the fascia and is then continued in the original direction through the skin of the other edge of the wound. Usually three such sutures are sufficient. The skin and subcutaneous tissues are packed open widely with kodoform gauze and silkworm gut sutures are held loosely in a hemostat (Fig. 3 a). The wound is then dressed. As a rule dressings do not need to be changed before they are removed for closure of the wound. After 48 hours the packing is removed and the previously placed silkworm gut sutures are tied sufficiently tightly to approximate the edges of the skin (Fig. 3 b). Some degree of edema of the edges of the incision will have occurred by this time and in our first few cases after the edema had subsided approximation of the edges of the wound was poor because

the silkworm gut sutures had been tied too loosely. This was easily corrected in subsequent closures.

After this method of delayed closure had been employed successfully for several months, it was thought that local use of one of the sulfonamide drugs might help in freeing the wound of some of the contaminating organisms. A first 5 grams of sulfanilamide was placed in the wound just before the packing but more recently the same amount of sulfathiazole has been used. We have not observed any difference in the healing of the wounds regardless whether a sulfonamide drug was or was not used but we are continuing to use it on theoretic grounds.

### RESULTS

To evaluate our results obtained after the described change of technique records concerning the last 47 primary closures and the first 47 delayed closures carried out on the same service by one of us (Pemberton) were reviewed. The operations in each group represented a consecutive series, but only typical operations of each type were included. Each in the investigation it became evident that the only significant differences between the two types of closure in so far as healing was concerned appeared in cases of fecal drainage. In cases in which there was no fecal drainage both types of wounds healed solidly and the time of healing as judged by the duration of drainage was the same. Twenty-nine primary closures in which there was no fecal drainage were entirely healed after an average time of 20.1 days and 33 comparable delayed closures were healed after an average time of 20.5 days (Table II). Fluid which drained from the wounds in both delayed closure was carried out as serious and came from the small regions of granulation tissue which resulted from the comparatively low closure employed as previously described. Fluid which drained in the cases in which primary closure was carried out originated from the site of the drain itself and usually became seropurulent before complete healing occurred.

*Spontaneous fecal drainage and primary closure.* Spontaneous fecal drainage was far more likely to occur after primary closure than after delayed closure and extensive infections were

the rule after primary closure when this particular complication developed. Of the 46 primary closures in which the bowel had been closed completely at the primary operation, spontaneous fecal drainage developed in 17. For the most part, the incisions became extensively undermined by abscesses containing pus and feces. Multiple drainage points appeared along the thinned-out sutured incision, and it was necessary in some cases to open the incision somewhat to provide for more adequate drainage. Fever and malaise developed in some patients, and prolonged hospitalization with much local treatment in the form of hot compresses and irrigations was required. In 10 of the 17 cases of fecal drainage, drainage finally stopped after an average interval of 30.4 days. In 7 of this same group of 17 cases fecal drainage did not stop, and, when the infection finally subsided, a fecal fistula remained that required subsequent operative closure. In only one case was failure of the closure possibly due to an inadequately destroyed spur. Of considerable importance in this connection is the fact that after such extensive infections, the amount of scar tissue in the body wall is increased and subsequent attempts at closure are more difficult technically and more likely to fail.

*Spontaneous fecal drainage and delayed closure.* As compared to the 17 cases of spontaneous fecal drainage, included among the aforementioned 46 cases of primary closure in which the bowel had been closed completely at the primary operation, there were only 7 cases of spontaneous fecal drainage in the group of 40 cases of delayed closure in which the bowel was closed completely. The incisions in the latter cases differed markedly from those in the group in which primary closure had been done, in that undermining was rarely seen (1 case only) and there were no extensive abscesses. The edges of the incision remained firm, and fecal and purulent material usually came from a single region. Generally, there was no fever or malaise, and the patients were able to leave the hospital after a shorter interval. The only local treatment necessary was maintenance of cleanliness in the region by the use of irrigations and by changes of dressing.

*Fecal drainage and closure about a clamp.* It is possible, occasionally, to apply a crushing

clamp to destroy completely a small spur at the time closure is done. In such cases the clamp is left protruding from the incision, and the opening in the bowel cannot be closed completely. Fecal drainage occurs along the shank of the clamp, and in such cases persistent fecal contamination is present in the incision from the time of the operation onward. Our rather distressing experience with such closures around a clamp when the wound had been closed primarily led us to employ this method only rarely. In only 1 case in the last 47 cases in which primary closure was carried out was true primary closure around a clamp attempted. The incision healed satisfactorily after 28 days. Healing after delayed closure in cases in which spontaneous fecal drainage occurred was so satisfactory that more closures around a clamp were attempted, and in the series of 47 cases of delayed closure, closure around a clamp was done seven times. Healing of these incisions did not differ from the healing of those incisions in which spontaneous fecal drainage developed. In 11 of the 14 cases in which delayed closure was carried out and in which fecal drainage occurred, both spontaneously and after closure around a clamp, healing of the incision was complete after an average time of 26.3 days. Two incisions were still draining after 31 and 45 days, respectively, but both fecal fistulas which were present ultimately closed without need for additional surgical treatment. In only 1 of the 47 cases in which delayed closure was employed did the wound fail to heal, and it was in this case that a persistent fecal fistula remained. Subsequently, the fistula was explored surgically, and the failure was found to be due clearly to a large remaining spur. A crushing clamp was applied to this spur and the mucosa was freed up from the skin. Spontaneous closure ultimately resulted.

#### CONCLUSIONS

The incision remaining in the body wall after closure of a colonic stoma generally is contaminated by bacteria from the open bowel. Delayed closure of such incisions is definitely superior to primary closure of them. When delayed closure is employed, the incisions become infected less frequently and the infections are less extensive and require less treatment than

when primary closure is carried out. Fewer spontaneous fecal fistulas occur and there is less chance for closure to fail when delayed closure is used than when primary closure is used. Closure around clamps can be attempted with greater chance of success when closure of the incision is delayed than is possible when closure is primary. Our satisfactory experience with delayed closure of colonic stomas is in accord with the experience of others in the

management of other types of contaminated wounds.

#### REFERENCES

- COLLIER, F. A. and VALE, W. L. *Ann. Surg.* 70: 55-56
2. DUFFORTIER, J. J. *Surg. Gy. Obst.* 1913 6: 11
3. GIBBER, H. A. *Discussion Ann. Surg.* 1920, 304-305
4. HARRIS, H. H. *Bell. M. J.* 919, 11
5. POOL, E. H. *J. Am. M. Ass.* 9 9: 71 1915
6. WARREN, W. H. and DEAN, F. S. *System of Surgery* Vol. 1 p. 379 Philadelphia Lea Bros. & Co. 1916

## PANLARYNGECTOMY FOR ADVANCED CARCINOMA OF THE LARYNX

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**P**ATIENTS with advanced extrinsic laryngeal cancer present a distressing situation for which there is practically no hope for cure and for which conservative palliative procedures are usually of little avail. Pain is an outstanding complaint, difficulty with respiration is more or less constant unless there is a tracheotomy tube in place and the sanguinopurulent discharges add to the general discomfort.

In a series of 5 patients with advanced extrinsic laryngeal carcinoma in which irradiation therapy had been carried out but failed to control the growth the writer performed a radical surgical excision encompassing the gross limits of the tumor. While "cure" was not anticipated the clinical course in the limited series was such as to have justified the performance of this operation as a palliative measure there having been no clinical or roentgenological evidence of metastases beyond the cervical region at operation.

#### TECHNIQUE OF OPERATION

Operation is not attempted if the tumor mass-larynx is frozen to the vertebral column.

Avertin, a vertin and local anesthesia, or avertin and local and intratracheal ether anesthesia are the types of anesthesia used (the

anesthetist scrubbing up with the operative team).

1. A T incision is made with the horizontal segment just above and parallel to the thyroid bone (Fig. 1).

2. The skin and platysma flaps are elevated to the right and left.

3. The trachea below the isthmus of the thyroid gland is isolated and transected. The lower opened segment is brought into the lower angle of the wound and the tracheotomy tube is inserted. If the latter has been inserted previously the transection of the trachea is carried out above the tracheostomy site. A gauze plug is inserted into the upper segment of the transected trachea to prevent constant dripping of the secretions.

4. The infrahyoid group of muscles in the lower neck is transected.

5. First on one side the cervical chain of nodes are dissected en masse upward. One or the other jugular vein if closely associated with involved nodes is doubly ligated and transected in the lower neck, the upper segment being retracted upward. If metastatic nodes are likewise adherent to the common carotid artery the latter may also be doubly ligated and transected low in the neck. Prior to this step a rubber covered clamp is applied to the common carotid in the base of the neck.

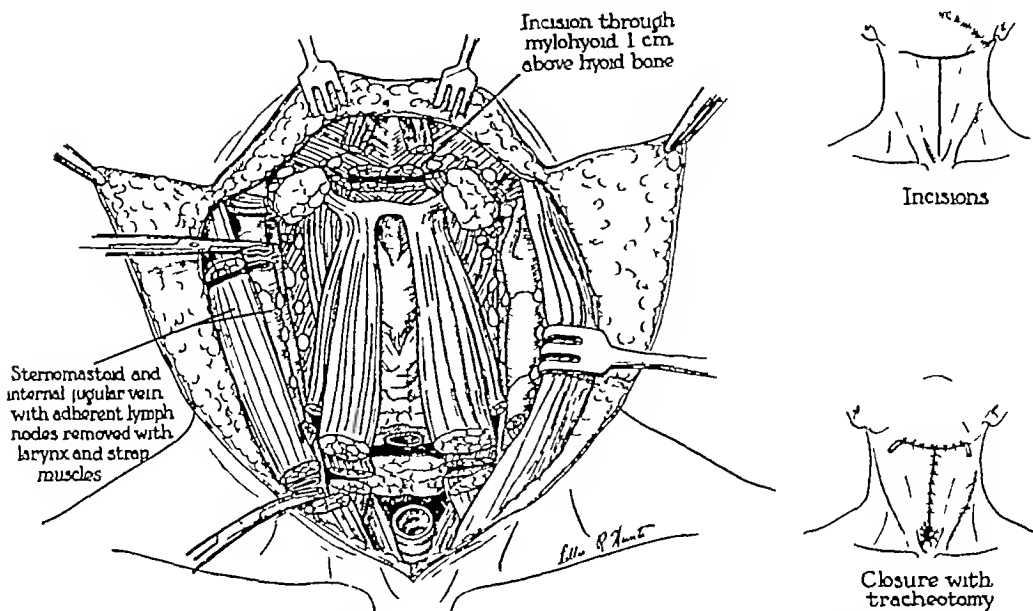


Fig 1 Schematic illustration of panlaryngectomy. The strap muscles are transected low in the neck, both bellies of the digastrics are cut, the submaxillary glands and nodes are dissected free *en masse* and reflected downward and toward the midline, the mylohyoid muscle is cut through into the pharynx. When a jugular vein and adherent carcinomatous nodes are to be excised with the larynx and attached muscles, the vein is transected low in the neck and as high in the neck as possible. To obtain a block excision, the sternomastoid is also freed by transection near its insertion and near its origin and removed *en masse* with the other structures excised. The trachea is divided below the isthmus of the thyroid and the lower end is brought up to level of skin. The upper half of the thyroid, or the upper portions of both poles adherent to the trachea is removed. At the completion of the operation the trachea is sutured to the skin with interrupted silk sutures, small rubber drains are inserted into each extremity of the horizontal portion of the incision and stab wounds may also be made in the lower portions of the neck on each side for drainage.

and pulse, blood pressure, and respirations are observed for 10 minutes. If there are significant disturbances of the latter, the clamp is removed, and the common carotid artery must be left *in situ*. When the jugular vein or carotid or both are to be removed, resection of the sternomastoid muscle on that side is likewise indicated (Fig 4).

6 If necessary the upper poles, or upper half of the thyroid gland, is freed from the lower portions and elevated with the tumor mass to be resected.

7 The tumor-mass-larynx is then freed by wide sharp dissection upward to the upper portions of the neck. The submaxillary glands and adjacent lymph nodes are freed first in the lateral portions of the submaxillary triangles in such a manner that they will be elevated medially and excised *en masse* with the larynx. The tissues in the submaxillary tri-

angles should not be excised as separate masses.

8 A transverse incision is then made through the muscles about 1 or 2 centimeters above the hyoid bone. This incision is carried through the base of the tongue into the pharynx.

9 The tumor-mass-larynx is then freed by widely cutting away the larynx from the hypopharynx. This may or may not entail removal of the epiglottis.

There remains only a strip of hypopharyngeal and upper cervical esophageal mucosa posteriorly. This varies from 1.5 to 2.5 centimeters in width depending upon the extent of laryngeal resection.

10 The hypopharyngeal and upper cervical esophageal mucosa are sutured as a tube over a Levine tube inserted through the nose into the esophagus by interrupted catgut sutures.





Fig. 2.



Fig. 3.



TABLE I—SUMMARY OF 5 CASES

Patient Age Case No	History	Present status	Operation	Postoperative course
I W M ♂ 55 yr (206882)	Carcinoma of larynx demonstrated by biopsy October, 1938—neoplasm involving left cord and quite large. History of hoarseness for 2 years. X ray therapy 4300 r surface dose in air, October–November 1938. Immediate improvement. Abscess developed in neck over larynx February 1939 drained. Sinus persisted, hoarseness aggravated.	Extensive firm induration palpable about larynx with sinus in midline from which neoplastic granulations protrude.	Panlaryngectomy 4–10–39 with excision of skin on anterior aspect of neck to include sinus. Epiglottis removed (Fig 3).	Satisfactory convalescence. Partial separation of wound but subsequent healing. Patient gained 50 pounds in weight since operation and has been doing physical labor. Satisfactory nutrition by mouth with liquid and semisolid foods. Survival since operation 4 years. No evidence of neoplasm (Fig 1).
II T L ♂ 47 yr (71533)	Carcinoma, base of epiglottis diagnosed by biopsy 8–8–38. X ray therapy August–September 1938 6655 r to two portals. Improvement. Recurrence with 2275 r X ray in June 1939. Tracheotomy November, 1939.	Marked woody induration about larynx. Carcinomatous mass involving larynx, hypopharynx and infiltrating surrounding tissues.	Panlaryngectomy, left jugular vein and sternomastoid also resected. Epiglottis removed <i>in toto</i> with larynx.	Postoperative course satisfactory. Operative wound partially separated but by end of 36th day postoperative could nourish himself by mouth with soft and liquid food. On 40th day while walking down hall in hospital sudden massive fatal hemorrhage occurred. Necropsy revealed this to have come from area in upper left common carotid artery invaded by tumor.
III A M ♂ 63 yr (239785)	Resection of papilloma of vocal cord and tracheotomy 9–10–39. X ray therapy Dec. 1939 to Jan. 1940 3100 r.	Large perilaryngeal tumor mass. Tracheotomy tube in place. Severe pain in larynx. Dysphasia.	Panlaryngectomy including resection of epiglottis 4–20–40. Convalescence complicated by bronchopneumonia.	Relieved of severe pain. Partial separation of operative wound. Gained 14 pounds in weight from September to December 1940. Neoplasm recurred in margins of wound. These were fulgurated to retard growth. By April 1941 cervical tumor mass had become quite large but there was no pain. Died at home April 20, 1941. No necropsy. Survived operation 1 year.
IV A. Y. ♂ 57 yr (243693)	X ray therapy to larynx (dose unknown in September 1939). Some pain in larynx and some dysphasia. Progressive increase in hoarseness.	Tumor mass involving larynx and palpable firm enlarged cervical lymph nodes bilateral.	Panlaryngectomy 6–25–40 including resection of epiglottis and left jugular vein.	Hemorrhage into upper portion of operative wound on second day necessitated its opening and packing with gauze. Subsequent convalescence satisfactory. Evidence of local recurrences November 1940. Excision of local recurrences on several occasions. Plastic closure of defect in neck by skin flap from shoulder. Radium implantations about individual recurrent masses resulted in their temporary shrinkage. Recurrences finally out of control and patient died of hemorrhage 1–2–42 from large infected neoplastic mass in neck. He had survived 19 months following the operation.
V D S ♂ 59 yr (138700)	Biopsy of lesion in larynx 10–22–35 revealed carcinoma. X ray therapy October–November 1935 to larynx total dose 4240 r. This was followed by regression of lesion. Hoarseness did not improve. Tracheotomy in July, 1941 because of acute respiratory difficulty. Developed tracheoesophageal fistula necessitating gastrostomy 11–1–41.	Firm swelling palpable about larynx. Fungating tumor mass replacing larynx. Metastatic nodes palpable in both upper cervical regions. Intense pain in neck radiating to head.	Panlaryngectomy 11–13–41. Jugular veins not resected.	Convalescence satisfactory. Wound separation. Patient fairly comfortable and previous pain relieved. Small nodules of recurrent carcinoma in margins of wound observed January 4, 1942. These and subsequent recurrences excised. Period of weight gain December 1941 to February 1942. Frequent small hemorrhages March and April, 1942. Died May 19, 1942 from massive hemorrhage. Necropsy not performed. Survived operation 6 months.

Although a large esophageal sinus and tracheotomy may be present in the neck, the patients learn to tube-feed themselves, are ambulatory, and learn to get along quite well wearing a relatively small gauze dressing over the anterior aspect of the neck. Frequently the tracheotomy tube is dispensed with (Fig 6).

The question of speech does not present a serious problem since speech can hardly be recognized to exist prior to the operation in view of the extensive lesion present.

The cases in which the procedure was performed are briefly summarized in Table I. In each instance the patient appeared quite ill prior to operation. All 5 patients subjected to panlaryngectomy experienced a period of increased comfort after operation and there were no immediate postoperative deaths. In Case 1, patient lived 48 months (is still clinically well, neck healed, normally active), in Case 2, patient lived 36 days and died from sudden massive hemorrhage, in Case 3 patient lived 12 months, in Case 4, 19 months,

and in Case 5 6 months these latter 3 all died with recurrence.

**Nutrition** Because of the wide resection of the anterior wall of the cervical esophagus tube feedings are necessary. Levine tubes are passed into the esophagus through the nose or directly into the esophageal anus in the neck. Maintenance or even gain in weight was possible by suitable tube diets. In Case 1 complete closure of the neck wound was possible. In Case 5 there was also a gastrostomy and while it might appear that a patient with both a tracheotomy and gastrostomy might represent an individual who "may just as well be dead" his existence during most of the postoperative period was far more comfortable than it was prior to operation when he had a very painful laryngeal neoplasm and tracheo-esophageal fistula. During most of the period of survival he was ambulatory and even did light physical work at times. In this connection the question of prolongation of life in patients with advanced carcinoma presents itself. It is the surgeon's duty to employ, with judgment, all measures which may pro-

long life in patients with advanced carcinoma provided it may be reasonably expected that the added period of existence will be spent in greater comfort than that prior to the operation and that the patient will not be made to lead a purely "vegetative" existence. No other justification for attempting resection of

inoperable carcinomas in patients in whom there is no evidence of distant spread is the fact that it is not very uncommon to observe unusually prolonged survivals with cure in patients who have had malignant neoplasms resected but in whom conditions were such at the time of operation that the surgeon had every reason to be very pessimistic as to the subsequent duration of life.

#### SUMMARY

Partial laryngectomy was performed to remove advanced extrinsic carcinomas of the larynx in 5 patients who had previously received x ray therapy which had not eradicated the neoplasm. The palliative results observed justify the procedure carried out in this group of patients.

# THE EFFECT OF SECTIONING VARIOUS AUTONOMIC NERVES UPON THE RATE OF EMPTYING OF THE BILIARY TRACT IN THE CAT

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NOTWITHSTANDING the intensified interest and the great progress made in the field of biliary physiology during the last two decades, the 1925 dictum of A. J. Carlson still stands "As regards the extrinsic nerve control of the contraction of the gall bladder and the musculature of the bile passages, and particularly the sphincter of Oddi, there are few fields in experimental physiology in which so much serious work has been done with so few conclusive results"

In partial explanation of this situation it may be noted that only comparatively recently has it been realized that the mechanism of evacuation may be primarily hormonal, so that the problem is not whether nerves cause or prevent emptying but to what degree, and how the autonomic nervous system modifies the activity of the biliary tract. Second, there is a surprising paucity of detailed information about the nerve supply of the biliary tract. Third, the experiments have been mostly acute experiments, "fighting Nature out of her usual bias" (to quote Robert Hooke), and thus not permitting analysis of natural functions under conditions approaching those to be found in the intact animal.

In the attempt to meet some of these deficiencies, Schulze and Boyden (1943) investigated the innervation of the biliary tract in the cat, an animal in which reflex inhibition of the gall bladder can be induced by faradic stimulation of the gut from stomach to cecum (Birch and Boyden, 1930). By employing a modification of the Wharton-Siehl technique of stretching a given nerve field on a flat surface, staining it *in toto* with Ehrlich's hematoxylin, decolorizing it, and dissecting

the nerves in glycerine with the aid of a binocular microscope, two independent pathways to the choledochoduodenal junction were discovered—a *gastroduodenal plexus*, lying between the artery of that name and the common bile duct, and a discrete *gastroduodenal nerve* which descends from the hepatic plexus a little to the left of the gastroduodenal artery (Fig 1). It was the finding of this nerve, whose components could be traced to the right vagus and both celiac ganglia, that suggested to the senior author the possibility of interrupting the pathways to the choledochoduodenal junction and of ascertaining how this affected the rate of emptying of the biliary tract in the unanesthetized and postoperatively recovered animal.

## EXPERIMENTAL AND OPERATIVE PROCEDURES

The first experiments were designed to interrupt the specific pathways to the choledochoduodenal junction—namely, the gastroduodenal nerve and plexus.

A cat, which had had no food for at least 12 hours previous to the operation, was brought to surgical anesthesia with ether and the body cavity was then entered through a midventral incision. The stomach was retracted inferiorly to expose the lesser omentum. The omental bursa was entered by passing through the gastrohepatic ligament. Then the hepatic artery was picked up in the right gastropancreatic fold and the gastroduodenal nerve located just caudad to the hepatic artery (Fig 1). The nerve was followed to the right as far as the origin of the gastroduodenal artery to be certain that it had received all its components. At this point in its course, as it lay just to the left of the gastroduodenal artery, it was severed or doubly ligated. A complicating factor here was found to be a large and quite constant lymph node

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Prepared for presentation before the Forum on Fundamental Surgical Problems, 1942 Clinical Congress of the American College of Surgeons, which was cancelled because of the war.

(one of the hepatic chain) situated in the angle formed by the hepatic and gastroduodenal arteries. This node lay superficial to the gastroduodenal nerve often completely concealing it and had to be reflected. Next the tissue to the right of the gastroduodenal artery was isolated down to the portal vein and the anterior surface of this vein was stripped clean of loose connective tissue and nerve plexus. The posterior and medial wall of the common bile duct at the level of the origin of the gastroduodenal artery were also stripped care being taken not to traumatize the common bile duct. Two ligatures were passed through the opening thus made and tied tightly so that the gastroduodenal artery and its surrounding gastroduodenal plexus were doubly ligated. In view of the thickness of the supporting tissues, this procedure was considered to be adequate to prevent impulses from passing to the choledochoduodenal junction over these specific nerves. Incidentally ligation of the artery did not produce any visible deterioration in the duodenum. This was also the experience of Bergh (personal communication) who found that any two of the arteries to the stomach could be ligated without producing gangrene.

In the second set of experiments the dorsal (s. right) vagus nerve was severed at the point where it emerges from the diaphragm with the primary object of interrupting its main contribution to the gastroduodenal nerve. Incidentally this also eliminated fibers supplying the gall bladder and stomach. Subsequently in other cats, as a control experiment, the ventral (s. left) vagus was severed at the same level the right vagus being left intact.

In the third series of operations the thoracic autonomic supply to the biliary duct system was eliminated. For this procedure, medium-sized to small cats were found to be the most suitable. The body cavity was again entered through a midventral incision. The greater and lesser splanchnic nerves were picked up and sectioned in their course from the diaphragm to the celiac ganglia. On the left side the ganglion lies just median to the left adrenal gland and spread upon the superior mesenteric and celiac arteries near their origin from the aorta. On the right side the

ganglion usually lies deep to the upper pole of the right adrenal gland.

In variations of this procedure in which the lumbar sympathetic trunk or lumbar roots of the celiac ganglion were picked up as they lay in the crevice between the crura of the diaphragm and the psoas muscles, it was found advisable to tear the parietal peritoneum and renal fascia above the kidney and to retract this organ inferiorly in order to make the operative field adequate. Also, to expose the desired nerves (especially the lumbar roots of the celiac ganglia) for sectioning, it was usually necessary to doubly ligate and sever the large adrenolumbar vein. The right side presented the most difficulty for two reasons: first the right celiac ganglion was often concealed by the adrenal gland or the inferior vena cava, or by mesenteries running to the vein from the liver; second the attachment of the caudate process of the liver so near to the ganglion made it virtually impossible to expose this nerve without traumatizing the liver. However the resulting hemorrhage was readily stopped by packing.

In other experiments, nerves were sectioned in various combinations to be described later.

After the nerves had been severed in each animal an insulated electrode previously prepared according to the method of Burk and Boyden (1930) was sewed to the greater curvature of the cecum. This consisted of the divided ends of two enamelled wires enclosed and tied into a small-gauge, flexible rubber tube. (Note silhouette of wires in Fig. 2.) At the end containing the electrode the tube had been split lengthwise for a short distance and its upper half discarded. At the time of operation the other half in which the electrode rested, was inverted and sewed by its outer to the cecum. The undivided end of the tube was then brought out through the laparotomy wound the wires connected to an induction coil, and the apparatus tested on the operating table. Closing of the circuit produced a ring-shaped spasm of the cecum at the level of the electrode.

The last step consisted of rendering the full bladder opaque to the x ray. According to the method of Whitaker (1936), an avascular spot on the fundus was perforated with a 27-gauge

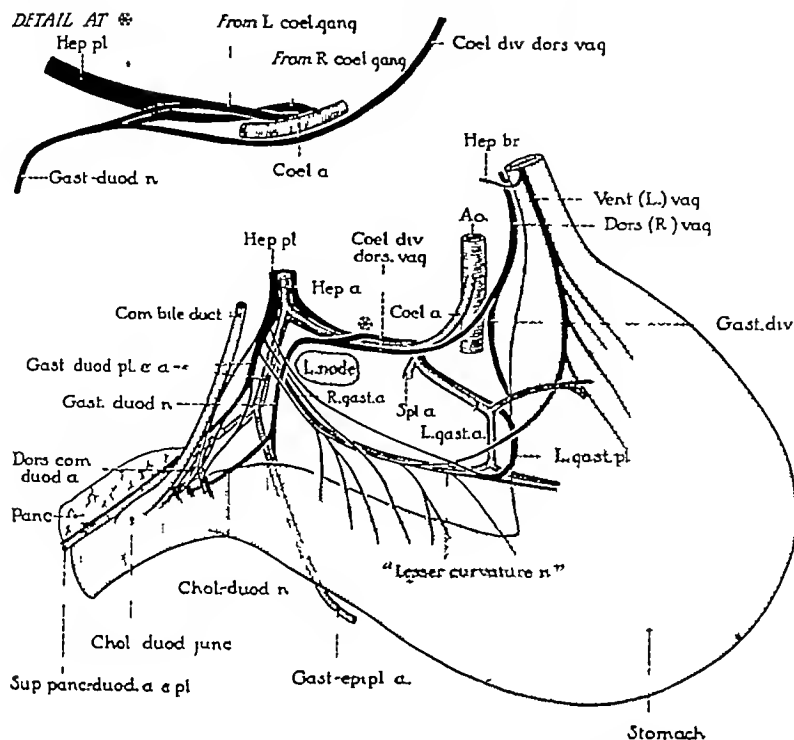


Fig 1 Diagram of the innervation of the biliary tract in the cat (after Schulze and Boyden, 1943) In the region of the bile duct the structures have been drawn as if somewhat spread apart, in order to display them better

needle, the bile milked from the gall bladder, and the latter filled to its original size with lipiodol—an iodized vegetable oil

The body cavity was then closed and the rubber tube with its contained wires led to the outside through the incision. By means of this arrangement, it was possible to stimulate the cecum in the unanesthetized animal some 15 hours after operation and to see how section of various nerves affected the reflex from gut tract to gall bladder and whether this involved the sphincter

Immediately after the operation, two roentgenograms were taken to determine the condition of the gall bladder. The next morning, 12 to 16 hours after the operation, when the cat had fully recovered and was moving about, another picture was taken to make certain that the gall bladder had not emptied during the night. The cats were then fed a meal of two egg-yolks and milk by gavage. Strangely, this meal usually soothed and pacified the cats

so that soon after being placed on the x-ray table and petted, they began to purr

Immediately after the meal, pictures were taken at short intervals to determine when the gall bladder came into tonus and when it first started to empty. When it was established that the column of lipiodol had reached the cystic duct a picture was taken, then a faradic current (with induction coil set at 4 cm) was sent into the cecum for 10 seconds. Forty-five seconds after the first picture a second was taken. Then another current was sent in and 45 seconds after the second current, or a minute and a half after the first, a third picture was taken. These were then studied to determine the presence or absence of the inhibitory reflex

As a control experiment, the wound and skin of the belly wall of the same cats in which the inhibitory reflex had been demonstrated, were pinched with forceps, or faradically stimulated, and x-ray pictures were

TABLE I—NORMAL RATE OF EMPTYING OF GALL BLADDER IN 12 CATS

Cat	Latent tension mm.	Oil enters cystic duct mm.	Rate of evacuation of gall bladder (mm. after last)		
			1/2 empty min.	1/2 empty min.	Empty, sec.
A — Group					
12	—	0—	40+	41	44
11	0—	0—	1.5 <sup>0</sup>	3	30
20	—	—	1 <sup>0</sup>	18	25
24	—	12	30 <sup>0</sup>	—	102
24	0+	—	30 <sup>0</sup>	40 <sup>0</sup>	100
—	—	12	1.5 <sup>0</sup>	43—	48
25	—	—	45	25	121
A	42 g/1 —	42 g/10 <sup>0</sup> —	1100 g/14 <sup>0</sup>	1100 g/17 <sup>0</sup> —	1100 g/17 <sup>0</sup> —
B — Group					
22	—	21	15	35	120+
—	26	20	24	17	46
24	—	—	2.5 <sup>0</sup>	200	311+
—	4—	20	1.50 <sup>0</sup>	24	170
27	0	—	60	30 <sup>0</sup>	30 <sup>0</sup>
Av	25 g/17 25	42 g/132 30	507 g/34 240	1000 g/100 200	1070 g/100 240
A (4, 4, 2)	42 g/4 <sup>0</sup>	30 g/100 g/20 <sup>0</sup>	1.50 g/170	40 g/1100	1070 g/110

Data reconstructed from tables and figures of DuBois and Hunt, 1932.  
<sup>0</sup>Estimated by interpolation.

taken at the same time intervals as before (viz. Fig. 2 second row) thus to eliminate the possibility that certain results could be explained on the basis of a cutaneovisceral reflex or that the change in shape of the gall bladder had been due to mechanical pressure caused by the struggling of the animal in response to pain. Also the induction coil was buzzed for 3 seconds without sending the current to the cecum to determine the presence of a conditioned reflex.

When the gall bladder was empty or nearly so the cat was sacrificed an autopsy was done, and drawings were made to record exactly which nerves had been cut and which remained.

Records were kept of the emptying time of the gall bladder and compared with the data of DuBois and Hunt (1932) who established the rate of evacuation of the gall bladder in normal cats following a meal of egg yolk.

#### OBSERVATIONS

1. *The normal rate of emptying in the cat.*  
 The only adequate information regarding the

normal rate of emptying of the gall bladder in mammals other than man is that supplied by DuBois and Hunt (1932) for the cat and the opossum. This was obtained by opening the body cavity expressing the bile through a small aperture in the fundus, and refilling the gall bladder with an iodized oil opaque to the x-ray. Some 12 to 15 hours later when the animals were in apparently good condition walking around and purring—they were fed (by gavage) a standard meal of three to five egg yolks and 30 to 50 cubic centimeters of cream, then x-rayed at frequent intervals until the gall bladder was completely empty.

In addition to tables, the authors published a series of silhouettes of each gall bladder. By using these figures, a table has been reconstructed which supplies additional information and makes possible a direct comparison with the data presented in this thesis.

A study of Table I emphasizes the findings of DuBois and Hunt, namely that the 12 cats fell into two series A a group of 7 in which the gall bladder emptied approximately 170

thirds of its contents in an average of less than 40 minutes after eating, and *B*, a group of 5 animals in which the principal period of discharge was spread over a period of some 3 hours, in such a way that the two-thirds mark was not reached until an average time had elapsed of over 198 minutes after food. No experimental analysis of these variations was attempted, but the present experiments suggest that in addition to the varying reaction of the animals to the shock of operation, the varying balance of sympathetic and parasympathetic control may have been a factor.

In comparing these figures with the data presented in this thesis, the average figures for all 12 animals of DuBois and Hunt have been used.

In concluding this section, it should be stated that the relative size of the gall bladder at different intervals was estimated by inspection of roentgenograms, according to simple rules based on the ratio of areas to volumes in the large series of human cholecystograms made by the senior author. While this method would not be sufficiently accurate to detect small differences, it has seemed adequate to reveal any gross differences in rate of emptying following excision of nerves.

2 *Effect of eliminating specific nerves to the choledochoduodenal junction.* As here outlined, the attempt was first made to eliminate all nerve fibers in the hepatoduodenal ligament converging upon the choledochoduodenal junction. But in 3 of the 11 cats in which the gall bladder reacted to food, although the gastroduodenal plexus was cut, the nerve was missed. In these 3 animals, therefore, the gastroduodenal nerve continued to function. Under these conditions the rate of emptying of the gall bladder seemed to compare favorably with the control data given by DuBois and Hunt (1932) for cats with intact nerves. As noted in Table II, A (cf Fig 2, row 1), the average time that elapsed before the gall bladders began to exhibit tonus was 6 minutes after food (controls, 9 minutes Table I), the average time required for iodized oil to enter the cystic duct was 23 minutes (controls, 20 minutes), and the time required to empty the gall bladder was 275 minutes (controls, 269 minutes).

But when the gastroduodenal nerve was eliminated in addition to the fibers of the plexus, then a very different picture was presented—namely a marked retardation in rate of emptying (see averages for 8 animals in Table II, B and compare with Fig 3, row 1). In fact the time required for emptying half or two-thirds of the contents of the gall bladder, was almost doubled from an average of 71 and 119, respectively (Table II, A) to an average of 165 and 232 minutes (Table II, B). While the number of animals in the first group is small, there is little overlapping of volumes, most of those for the second group being higher than comparable ones in the first group.

These observations, therefore, indicate that the gastroduodenal nerve carries fibers which lower the resistance at the biliary outlet. Further evidence that such fibers do not pass by way of the gastroduodenal plexus is that in animals 8, 9, and 12 of Table II, B, some fibers of the plexus escaped the ligatures, yet emptying of the gall bladder in these 3 was nevertheless retarded. The practical application to be made from these experiments is that severance of nerves to the choledochoduodenal junction in human patients should not be expected to lower the resistance to the flow of bile but rather to increase it.<sup>1</sup>

Turning now to the experiments on faradic stimulation of the cecum, it is clear that severance or ligation of the gastroduodenal nerve or plexus, or both, failed to affect or to abolish the inhibitory reflex from cecum to gall blad-

<sup>1</sup>The first attempt to relieve the pain of biliary dyskinesia in man by sectioning nerves in the hepatoduodenal ligament was performed by Reich (1940) in a patient that was being choledochostomized. Ten days after operation the intraductal pressure was found to be 85 millimeters of saline—30 millimeters less than the pressure obtained before operation. Injection of a quarter gram of morphine then caused a precipitate rise in pressure to 220 millimeters. Because this was not maintained for several hours as in patients with an intact sphincter, the author concluded that the 85 millimeter level represented a residual pressure due to the tone of the duodenum and that excision of the nerve in this instance had relieved spasm of the sphincter.

Until this single experiment has been verified there are several *a priori* objections to it. First the average level of intraductal pressure in 11 choledochostomized patients was found by Bergh and Layne (1942) to be 120 millimeters of saline and to range from 110 to 140 millimeters. In another article of the same date Bergh showed that after cystic jolt the average fall in resistance was 70 millimeters, and that in one instance a spastic sphincter was lowered from 450 to 110 millimeters in 30 minutes. Therefore it would not seem that Reich's drop of 40 millimeters in 10 days is significant. Second there is no evidence that severance of autonomic nerves affects the reaction of smooth muscle to morphine. Third, there is little known about the nervous pathways to the sphincter of Oddi in man, owing to the almost insuperable obstacle offered by the pancreas, so that in merely sectioning a nerve running horizontally behind the hepatic artery and approaching the bile duct just where it passes behind the duodenum there is no assurance that at this high level Reich may not have cut a nerve to the duodenum or pancreas.



TABLE II—EFFECT OF CUTTING NERVES TO CHOLEDOCHODUODENAL JUNCTION

Cat	Time of feeding—hrs. after operation	Initial tension in gall bladder mm.	Oil enters cystic duct mm.	State of evacuation of gall bladder—Minutes after feed				T-tension in gall bladder
				15 empty mm.	15 empty mm.	15 empty mm.	Empty mm.	
A. Gastroduodenal plexus cut or doubly ligated—Gastroduodenal nerve intact								
			6	40	12		175	not fed
6	24	2	40	—	—	175	172	
	1	2	2.5*	2.5*	1.20	175 (14)	171	
A. average		2.1 (6)	17 (22)	1.2 (12)	1.2 (10)	175 (14)	171 (12)	
B. Gastroduodenal nerve and plexus cut or doubly ligated								
	24	21		17 (11)	120	—	—	not tested
3	24	6	(Comms at 37)	not tested	—	—	—	
18	7	24	24	—	—	—	175 (12)	
14	23	13 +	24 (11)	—	—	—	175 (12)	
21	14	14	13	1.20	17	—	170	+
22	24	24	24	—	—	—	175 (12)	+
12	24	17	1.20	17	—	—	170	+
14	14	30	17 (11)	17	—	—	—	+
Average		21 (10)	12 (14)	1.2 (11)	1.2 (12)	175 (14)	171 (12)	

\*The  
line shows the gastroduodenal plexus was injured.  
Fractures in parentheses indicate nearest available reading.  
Bladder had been evacuated.

+ Plus signs in last column indicate degree of relaxation.  
\*(11) after 14 empty" column shows that only 11 of 14

der. In all of the 7 animals in which it was tried (see last column, Table II) the emptying of the gall bladder was stopped. The last 3 pictures in row 1 and the first in row 2 Figure 2 show how the column of oil in the cystic duct had dropped back within 45 seconds after the current had produced a spasm of the cecum, and how the gall bladder continued to relax after the second current was sent in. The middle 3 pictures of the second row show control experiments on the same animal and demonstrate that pinching the skin with forceps to produce the same amount of pain as spasm of the gut did not diminish the tonus of the gall bladder although a subsequent current lowered the tonus (last pictures in Fig 2). These roentgenograms were taken of an animal (cat 7) in which the gastroduodenal plexus had been eliminated but not the nerve of that name. Those in Figure 3 are from a cat in which the gastroduodenal nerve was severed but not all the fibers of the

gastroduodenal plexus (cat 9, cf Table II, B). Here it can be seen (last 3 pictures of first row) that the current produced marked dilation of the gall bladder whereas after pinching (first 3 pictures, second row) the phase of emptying apparently just started, was not inhibited. Subsequently induced spasm of the cecum caused marked fall in gall bladder tonus (last three pictures, second row).

These experiments would seem to prove, therefore that stoppage of flow of bile from the gall bladder as a result of visceral pain is not dependent upon sphincter action and is not necessarily initiated by it, since the gall bladder can be inhibited in the absence of nerves to the cholechochododuodenal junction. Conversely Bergh (1912) has shown that in cholecystectomized patients, ingestion of egg-yolk will lower the initial resistance of the sphincter by an average of 7 centimeters of water. So it is apparent that both gall bladder and sphincter can work independently of

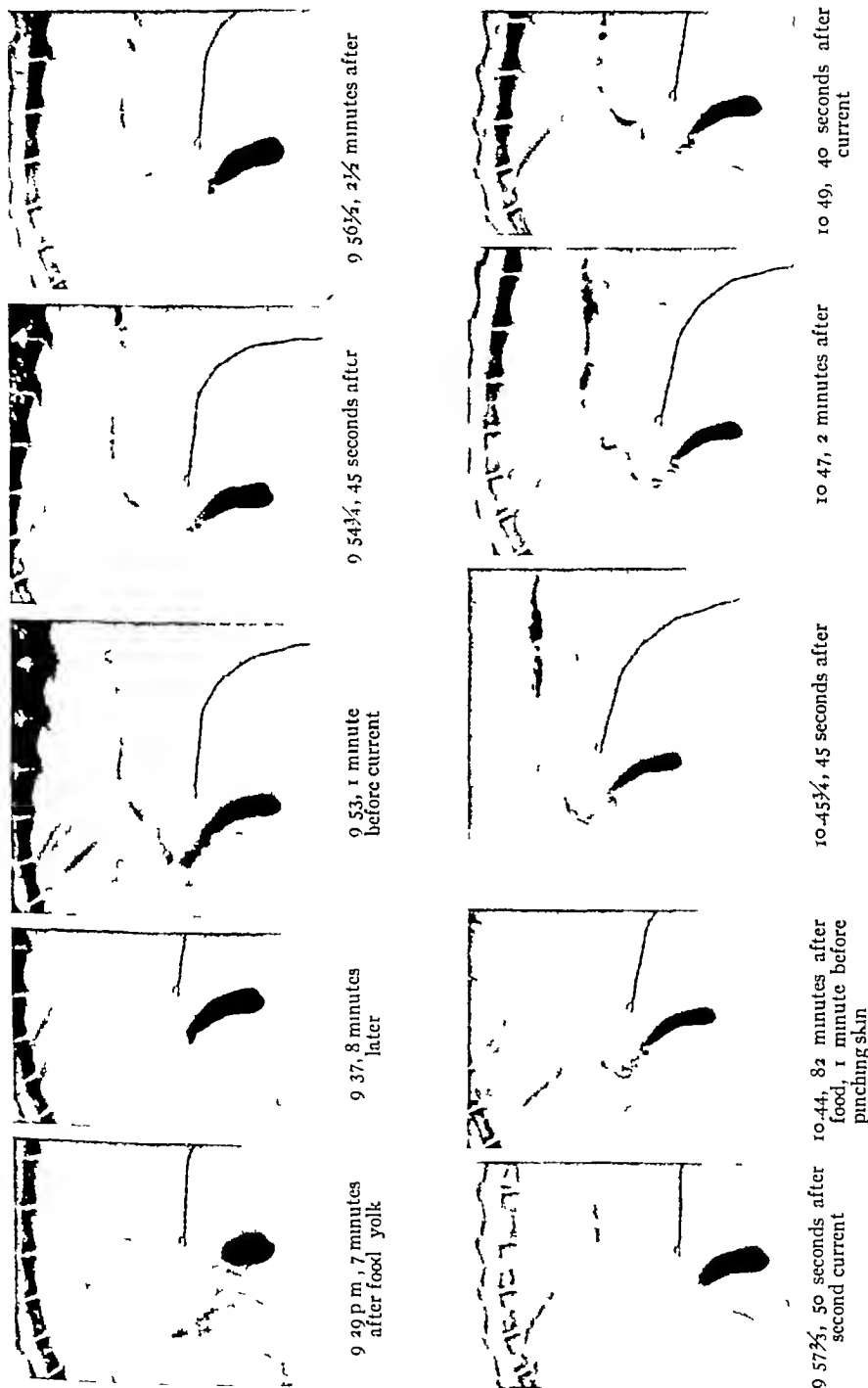


Fig 2 Roentgenograms of the emptying of the gall bladder in cat 7 (as viewed from left side) after the *gastrointestinal plexus* had been interrupted. Note that the rate of emptying was

not retarded (cf No 7, Table II, A) and that reflex inhibition of the gall bladder was not abolished, i.e. the column of iodized oil slumped (last two pictures, row 1) after faradic stimulation of

the cecum (position of the latter indicated by 2 pronged electrode). Pinching of the skin (middle three pictures, row 2) did not cause loss of tone in gall bladder

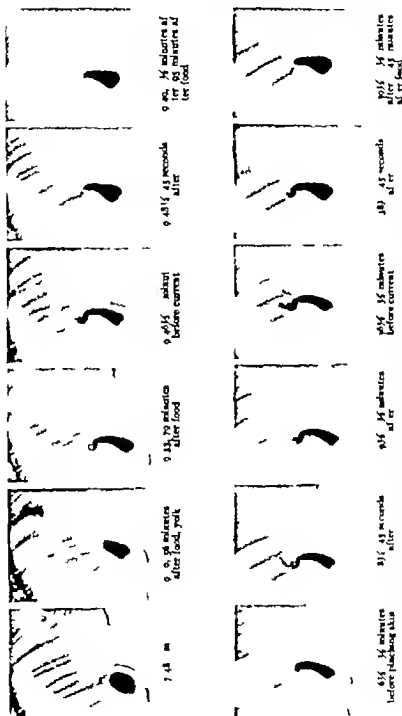


Fig. 1. Radiograms of the stomach of the cat, after the yolk had been introduced. The arrow had been introduced into the stomach.

may be ascribed to the fact that the stomach is not yet fully contracted (cf. N. 9, Table II B). As in Figure 1, inhibitory reflexes caused by stimulation of the stomach wall are not observed.

Stimulation of the stomach wall is not observed (last 3 sec. after, row 1) and from the beginning of the stimulation (first 3 sec. after, row 1) no reflex is observed (last 3 sec. after, row 1).

each other, i.e., there is no obligatory reciprocal mechanism<sup>1</sup>

3 *Effect of eliminating right or left vagus nerves* Since anatomically the dorsal (s right) vagus seemed to contribute the only vagal component to the gastroduodenal nerve (inset, Fig 1) and since severance of the latter retarded the flow of bile, it was next deemed advisable to study the effect of severing the right vagus nerve above the point where it divides into celiac and gastric divisions. The results of these experiments are shown in Table III, A and Figure 4

In 6 animals the average time required for iodized oil to enter the cystic duct was 95 minutes (as against 20 for the controls and 71 for animals with a severed gastroduodenal nerve). To empty half the contents of the gall bladder, 219 minutes were required (as against 70 for the controls and 165 for the animals in which the gastroduodenal pathway had been cut). Analyzing the figures in another way, it appears that in 5 of these animals (last column, Table III, A), the gall bladders were in continuous contraction for an average period of 3 hours, yet in that time less than half the contents as expelled. But in the 12 controls, continuous contraction emptied two-thirds of the contents of the gall bladder in half that time (89.5 minutes, as computed from the figures and table of DuBois and Hunt)

From these observations it is apparent that when the right vagus is cut, there is not only an increased resistance to the flow of bile at the sphincter, but also decreased contractile force applied by the gall bladder, for the rate of emptying is much slower when the right vagus is cut than when merely the gastroduodenal nerve is eliminated

This inference is substantiated by supplementary experiments in which the ventral (s left) vagus was cut subdiaphragmatically—a nerve which sends no components to the gastroduodenal nerve (Fig 1). In three such experiments (Table III, B) it was observed that it took an average of 152 minutes to empty half the contents of the gall bladder as against 219 minutes when the right vagus was cut, but that still the figure was much greater than the time required in the control animals (70 minutes, Table I)

The conclusions to be drawn from the above experiments are two (1), that both vagi augment the power of contraction of the gall bladder, (2), that in addition, the right vagus, through its celiac division, sends inhibitory fibers to the sphincteric mechanism<sup>2</sup>

4 *Effect of eliminating the splanchnic pathways* When all the splanchnic roots to right and left celiac ganglia were cut (7 animals, Tables IV, A and A', and Figure 5) the inhibitory reflex was abolished and the rate of emptying of the gall bladder was approximately that of the controls, i.e., half of the contents were emptied in an average of 86 as compared to 70 minutes, two-thirds emptied in 117 as compared to 104 minutes, and most of the contents in 238 as compared to 269 minutes (cf Table I). The time required for initial tonus and for the oil to enter the cystic duct was somewhat greater, although pictures were not taken at sufficiently short intervals to secure accurate data. But when one considers the much greater shock to which these animals were subjected (for even under light anesthesia the animals jump when these nerves are cut) and the fact that the inhibiting reflex from cecum to gall bladder was abolished when the sympathetic pathway was interrupted (removal of which inhibition

<sup>1</sup> DuBois and Kistler (1933) in an ingenious study of the biliary tract in guinea pigs found that when the extraduodenal ampulla of the bile duct as well as certain poorly defined cords of the lesser omentum posterior to the common bile duct were stimulated faradically, contractions of the gall bladder could be recorded (by means of a heart lever attached to the fundus of the gall bladder). Also that severance of the common duct prevented the stimulation of the ampulla from causing contraction of the gall bladder, but that the latter responded to excitation of the hepatic end of the cut bile duct and of the vagi. From these experiments they concluded that in the guinea pig there is a direct nerve connection between the ampulla and the gall bladder. In the light of our work on the nerves of this region it is suggested that in stimulating the omentum DuBois and Kistler may have been stimulating efferent branches of the left vagus (lesser curvature nerve) on their way to the gall bladder and that in stimulating the hepatic end of the cut bile duct they may have been stimulating afferent fibers of the gastroduodenal plexus adjacent to the bile duct (cf Fig 1). Since the guinea pig has this highly specialized pumping apparatus perhaps sensory nerves from the contractile ampulla play a rôle in regulating the activity of the gall bladder in this species.

<sup>2</sup> Although it has long been maintained that the vagi cause contraction of the gall bladder it has only recently been verified by neurohistological methods (Sabussow and Susulikow 1937). Forty-eight hours after section of the vagi in the dog these authors removed the gall bladder stained it with the Bielschowsky-Gros method and found a degeneration of the pericellular apparatus which embraces the ganglion cells lying external to the muscular tunic of the vesicle. From this they concluded that the vagus is motor to the gall bladder. They also observed that when both the vagi and the celiac ganglia were eliminated the histological preparations of the gall bladder wall still retained some undegenerated postganglionic fibers. These were interpreted as being postganglionic to the intramural ganglia of the gall bladder. I.e., they belonged to the intrinsic nerve net. In this connection it should be recalled that when the biliary tract is stripped of all extrinsic nerves the gall bladder still empties in response to the hormones released by egg yolk (Whitaker 1926) although its rate of emptying under such conditions has never been determined.

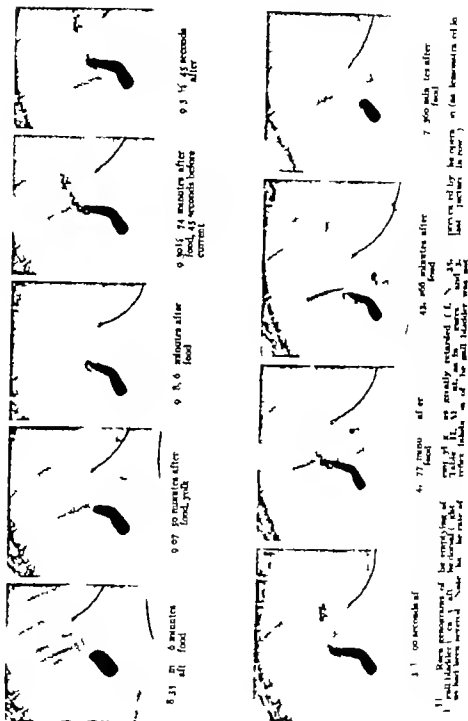


TABLE III—EFFECT OF CUTTING VAGI AT ESOPHAGEAL HIATUS

Cat	Time of feeding—hrs. after operation	Initial tonus in gall bladder min	Oil enters cystic duct min.	Rate of evacuation of gall bladder				Reflex inhibition of gall bladder	Period of sus- tained contraction* min
				½ empty min	¾ empty min	¾ empty min	Empty min		
A Right vagus (and its celiac division)									
15	14	44—	122+	216 (¾)	—	401	—	++	
35	19	50—†	61—	177+†	—	—	360 (¾)	++	205 (61—266)
17	20	48—	100‡	281	326	—	—	++	181 (100—281)
38	19	80‡	196	324	—	—	—	++	128 (196—324)
39	19	29—	37—	192 (¾)	—	—	347 (¾)	++	185 (37—222)
40	18	25	55+	126 (2/5)	155	188	218 (5/6)	++	199 (55—54)
Average		6)276(49)	6)571(95'	6)1316(219)					5)898(180)
B Left vagus									
41	18	22	78	192—	225	225	284 (¾)	++	114 (78—192)
46	15	15—	22	120—			338 (¾)		
42	18	9	45	135	152	221	280 (¾)	++	90 (45—135)
Average		3)46(15'	3)145(48)	3)456(152)			3)90 (301)		2)204(102)

\*During which gall bladder discharged continuously yet failed to empty more than half its contents

†Fig. 4

‡Emptying for 226 min. (100-326)

§Relaxes at 136 (emptying for at least 128 (196-324))

should increase the rate of emptying) it is probable that the slight reduction in the time required to nearly empty the gall bladder in this group of 7 animals should be interpreted as a slight acceleration of the rate of evacuation of the biliary tract

This is confirmed by the second group of 7 animals (Table IV, B and B') In these cats some of the fibers of the splanchnic pathway escaped section—either by way of the first and second lumbar roots of the celiac ganglia (B, Table IV) or in other types of experimentation (B') when a few of the anterior branches of the celiac ganglia escaped In such animals the inhibitory reflex from cecum to gall bladder was not abolished and emptying was retarded, i.e., when some of the fibers of the splanchnic pathway remained it took an average of 117 instead of 86 minutes to empty half the contents of the gall bladder, and 179 instead of 117 minutes to empty two-thirds of it. The difference is even more impressive if the comparison is restricted to the 5 animals in Table IV, B. Here the corresponding figures would be 132 to 86, and 212 to 117. (In the 2 animals recorded under B', in Table IV,

only a few fibers escaped section, but these were enough to preserve the reflex

The inferences to be drawn from these experiments are as follows. If section of the splanchnics may be considered to have somewhat accelerated emptying, the new rate must have been due to the fact that the operation abolished the inhibitory reflex from the cecum to the gall bladder.<sup>1</sup> The possibility remains, of course, that the splanchnics also maintained the tone of the sphincter and that when they were cut, the resistance was lowered and the rate of flow was thereby accelerated. However, since the acceleration was so slight and since section of the gastroduodenal nerve (through which the splanchnic fibers would pass) markedly retarded emptying, it is believed that some other agency than the sympathetic maintains the tone of the sphincter during fasting. It is suggested that this agency is local, perhaps the intrinsic nerve net

<sup>1</sup> Sabusson and Sushnikov have given us a neurohistological picture of what happens in the gall bladder of the dog when both celiac ganglia are extirpated. When the wall is stained for nervous element, degenerating bundles of myelinated nerves (afferent fibers?) and degenerating terminal synovia passing to the muscle fibers are found, but there is no degeneration of the pericellular apparatus around the ganglion cells. The authors interpret this to mean that postganglionic nerve fibers from the celiac plexus degenerate as far as the tissues in which they terminate



TABLE IV—EFFECT OF CUTTING SYMPATHETIC COMPONENTS

TABLE IV—EFFECT OF CUTTING SYMPLECTIC TRUNKS

Cat	Time of feeding—hrs. after operation	Initial tonus in gall bladder—min. after food	Oil enters cystic duct min	Rate of evacuation of gall bladder (min after food)				Reflex inhibition of gall bladder	Pain
				½ empty min.	¾ empty min	¾ empty min	Empty or nearly empty		

A All splanchnic roots to celiac ganglion cut (symp trunks intact)

23	13	5—	5—	21	36	62	104	—	—
24	12	3+	45+	105	123	197—	252 (5/6)	—	—
28	15	22—	33—†	56+	90‡	120 (4/5)	200 (5/6)	—	—
34	12	38—	38	72	95‡	118	209 (7/6)	—	—
33*	13	34—	34	123	133	215 (5/6)	275	—	+

A' All splanchnic roots to celiac ganglion cut, plus lumbar symp trunks

27	16	0	7†	52	120	155	206 (4)	—	—
26‡	10	17	118	175	226	291	360 (5/6)	—	—
Average		7)110(17)	7)40(34)	7)604(86)	7)823(117)	7)1158(166)	7)665(238)		

B Both major splanchnics cut (lesser and least splanchnics intact)

18	19	7—	22—	83	162	215	293 (9/10)	++	
20	15	20—	58—	98	163		163 (2)	++++	
22	14	80—	103—	151 (¾)	187	204+	204 (¾)	++	
31	12	23	40—	142 (1/10)	300	300 (2)	300 (2)	+	
32	10	40—	64	185 (1/5)	250‡	—	108 (5/6)	+	

B' Fibers of major splanchnics incompletely cut

19	18	19—	35+	66	80‡	—	158+	++	
29†	17	12—	47—	93	114‡	142	187 (9/10)	+	
Average		7)210(30)	7)374(54)	7)818(117)	7)1256(170)		7)1613(230)		

\*Except root from L1 and L2 sympathetic ganglion (Fig 6)

†Fig. 5

‡Established by interpolation

§Left lumbar sympathetic intact

||Left major splanchnic intact.

¶Anterior branches of celiac ganglia (leading to celiac artery) cut some fibers escaped

which surrounds the lower biliary passages (see figures by Schulze and Boyden, 1943) Indeed, it seems more reasonable to assume that in the long intervals of fasting the sphincter is kept closed by a local mechanism than by the intervention of extrinsic nerves

Apparently, also, the sympathetic excitation of the gall bladder is much weaker than the vagal, since the retardation caused by severing the vagus is much greater than the acceleration obtained by severing the splanchnics. In this connection it should be recalled that inhibition of the human gall bladder cannot be induced by faradic stimulation of the stomach and duodenum, as in cats (Boyden and Rigler, 1934). Also it is possible that in

man the vagus has lost its power to release the sphincter since its resistance is not lowered by neuromimetic drugs (Bergh, 2) and that this is accomplished only by antispasmodics and such hormone-producing substances as egg-yolk and magnesium sulfate (cf Boyden, Bergh, and Layne, 1943)

5 *Pathways of pain and of reflexes to the gall bladder from the cecum* Of special interest are certain incidental findings recorded in Table IV. First, in order to abolish reflexes from the cecum to the gall bladder it is necessary to cut both the major and the minor splanchnic nerves (i.e., to cut down to and include the rootlets of the first lumbar ganglion). Owing to variations it is probably



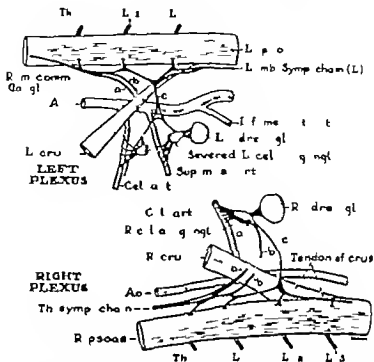


Fig. 6. Dissections made at autopsy of cat 33 (cf. Table IV, A). On both sides the greater *a*, and lesser *A*, splanchnics had been severed but not the least, *c*, splanchnic nerves. On the left side the celiac ganglion had also been bisected. Since, in this animal the inhibitory reflex to the gall bladder from the ceum had been abolished by section of nerves, it would have traversed the greater and lesser splanchnics. (The interrupted portion of this course is indicated by dotted lines). But pain following spastic contraction of the ceum, as not abolished, as less all splanchnics are severed (see other animals recorded in Table IV, A and A7); therefore pain impulses must have traversed the superior mesenteric plexus and least splanchnic nerves to have reached the brain segments of the spinal cord.

safer to cut the least splanchnics, also. But in order to abolish pain from the ceum it is necessary to cut all splanchnic roots as far down as the second lumbar sympathetic ganglion, i.e. not only the greater and lesser but also the least splanchnic nerve. Evidence for this is shown in Figure 6 comprising drawings made at autopsy of Cat 33. In this figure the left plexus is drawn from the left side with the cat lying on its right flank; that of the right plexus from the right side with the cat rolled over onto its left flank. On both sides the major *a* and minor *b* splanchnics have been cut but the least *c* escaped. Under these conditions the inhibitory reflex was abolished but the pain still persisted. This suggests that the pain impulses reached the spinal cord through the superior mesenteric plexus, the

least splanchnic nerve and the rami communicans of the second lumbar.

Second these findings are contrary to the observations of Kuntz and Van Buskirk, who reported that complete decentralization of the celiac ganglia of the cat following bilateral section of splanchnic and vagus nerves, does not abolish another type of inhibition of the biliary system, namely secretion of bile during fasting. This inhibitory reflex is elicited by distention of the ileum and colon (Goldman and Ivy, 1939) or by faradic stimulation of the inferior mesenteric plexus. From such experiments Kuntz has inferred that reflexes may pass from the large bowel to the biliary tract without entering the spinal cord or traversing the splanchnic nerves, i.e., that such reflexes are mediated by the celiac ganglion. Is it

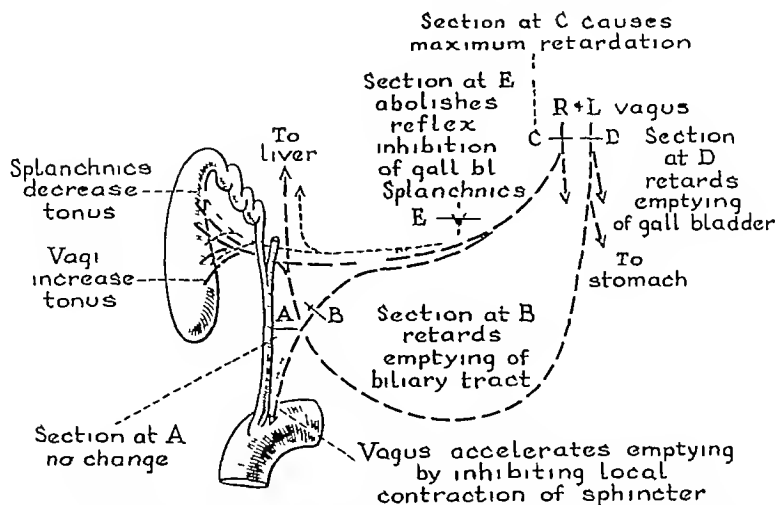


Fig 7 Diagram summarizing the effects of sectioning various autonomic nerves (cf summary in Table V) Area A, gastroduodenal plexus, B, gastroduodenal nerve.

of our difficulties in securing all the filaments, one wonders if the persistence of the reflex, as described by Kuntz, may not have been due to the failure of the operator to intercept all splanchnic nerves

#### SUMMARY AND CONCLUSIONS

The effects of cutting or otherwise eliminating certain nervous pathways to the biliary tract in 34 cats are represented graphically in Figure 7 and assembled in Table V. They may be summarized as follows:

Severance of the gastroduodenal *plexus* to the choledochoduodenal junction does not

affect the rate of emptying of the bile passages after ingestion of food nor abolish the inhibitory reflex to the gall bladder from the cecum. Presumably this plexus consists of afferent and vasomotor fibers.

Severance of the gastroduodenal *nerve* which innervates the same junction, markedly retards emptying. These observations raise serious doubt as to the efficacy of severing the nerves in the hepatoduodenal ligament of man as a means of treating a spastic sphincter, as recommended by Reich (1940).

Severance of the right vagus (and its celiac division) produces even greater retardation of

TABLE V—SUMMARY OF RATE OF EVACUATION OF GALL BLADDER FOLLOWING SECTION OF NERVOUS PATHWAYS

Nervous pathway interrupted	No animals	Initial tonus min	Oil enters cystic duct min.	1/5 contents gall bladder discharge min.	3/5 discharge min	All discharge min	Reflex from cecum to gall bladder	
							Reflex	Pain
Lipoidol controls (DuBois and Hunt)	12	0 <sup>3</sup>	20 <sup>10</sup>	70	104	269	Not attempted	
Gastroduodenal plexus	3	6 <sup>2</sup>	23	71 <sup>2</sup>	119 <sup>2</sup>	275	+	+
Gastroduodenal nerve	8	26	71	165 <sup>1-2*</sup>	234 <sup>1</sup>	373 <sup>1-†</sup>	+	+
R. vagus	6	49	95	219	—	—	+	+
L. vagus	3	15	48	152	—	301 <sup>1-†</sup>	+	+
All splanchnic roots of celiac ganglion	7	17	34	86	117	238 <sup>1-†</sup>	0	0
Most splanchnic roots (some escaped section)	7	30	54	117	179	230 <sup>1-†</sup>	+	+

Exponents indicate number of animals used in computing averages when below full number  
<sup>1</sup>3 only 1/5 discharge. <sup>†</sup>2 only 1/5 to 3/5 discharge. <sup>‡</sup>Only 1/5 to 3/5 discharge.

<sup>1</sup>2 only 5/6 <sup>1</sup>4

<sup>3</sup>3 only 1/5-3/4.

flow from which it is inferred that the right vagus not only sends parasympathetic inhibitory fibers to the sphincter region via the gastroduodenal nerve, but also motor fibers to the gall bladder via the hepatic plexus. The latter inference is substantiated by the fact that severance of the left vagus (which does not send fibers to the choledochoduodenal junction) also retards the emptying of the gall bladder but to a lesser degree.

Severance of the splanchnic roots of the celiac ganglia as far down as the second lumbar nerve abolishes the inhibitory reflex from cecum to gall bladder thereby somewhat accelerating the emptying of the gall bladder. Since cutting the nerve to the sphincter (gastroduodenal nerve) does not accelerate the flow but retards it presumably this nerve does not convey sympathetic fibers charged with maintaining the tone of the sphincter. It is suggested therefore that during fasting the biliary outlet is kept closed through the action of a local mechanism perhaps the intrinsic nerve net, and that after meals the tonic contraction of the sphincter is overcome by the right vagus and by hormones being formed in the intestinal mucosa. Since, in human patients the neuromimetic drugs have so little effect upon a spastic sphincter it is possible that in man the vagus has lost its power to release the sphincter and that this is accomplished only by antispasmodics and hormone-producing substances.

These experiments also indicate that in the cat there is no obligatory reciprocal relationship between gall bladder and sphincter since each responds to appropriate stimuli when the nerve to the other is cut. The vagus aug-

ments the tone of the gall bladder and its contraction of the sphincter (thereby accelerating the flow of bile) the sympathetic exerts a temporary inhibiting effect on contraction of the gall bladder—a function that is apparently absent in man—thereby retarding the flow of bile from a viscus that is emptying under the influence of hormones and emanations from the vagus.

Pain impulses from radically indurated spasms of the cecum enter the spinal cord as low as the second lumbar ganglion, having traversed the superior mesenteric plexus and the least splanchnic nerves.

#### REFERENCES

1. BYRON, GEORGE S. *Am. J. Digest. Dis.*, 1941 6 40-5.
2. *Ibid.*, *Surgery*, 1942, 300-330.
3. BYRON, GEORGE S. and LAYNE, JOHN A. *Am. J. Digest. Dis.*, 41 9 62-65.
4. BYRON, CARROLL L. and BOYD, EDWARD A. *Am. J. Physiol.*, 130, 9 301-3 6.
5. BOYD, EDWARD A. *Anat. Rec.*, 93, 20 57-72.
6. BOYD, EDWARD A., BYRON, GEORGE S. and LAYNE, JOHN A. An analysis of the reaction of the lower gall bladder and sphincter of Oddi to sodium sulphate. *Surgery* 413 (1942).
7. BOYD, EDWARD A. and G. UTTER, *J. Surg. & Gyn. Obst.*, 1936, 6 34-42.
8. BOYD, EDWARD A. and REIGER, LEO G. *Am. Rec.*, 1934, 99 477-487.
9. CARRISON, A. J. *J. Am. M. Ass.*, 1935, 85 1474-1475.
10. DUNN, F. S. and HUNT, E. A. *Anat. Rec.*, 112 44 250-306.
11. DUNN, F. S. and KETTER, G. H. *Proc. Soc. Exp. Biol., N.Y.*, 1935, 30 78 80.
12. KETTER, A. and V. BOTTELDOORN, C. *Proc. Soc. Exp. Biol., N.Y.*, 1941, 45 510-513.
13. REIGER, HERBERT. *Surg. Gyn. Obst.*, 1936, 77 397-405.
14. SUTHERLAND, G. H. and SUTHERLAND, A. F. *Lancet*, 1936, 1 837 66 739-743.
15. SCHILLER, JOHN W. and BOYD, EDWARD A. The innervation and blood supply of the choledochoduodenal junction. *Anat. Rec.*, 943 (1942).
16. W. UTTER, L. R. *Anat. Rec.*, 1937, 87 454-473.
17. WITTAKER, LEWIS R. *Am. J. Physiol.*, 1925 75 6 435.



surgical therapy. Among these we find leiomyomas of varying size usually the smaller ones. Such tumors were the chief reason for operation in 170 cases. Prolapse is stated as the reason for operation in 144 cases. Many of these were extreme cases in which the uterus came well outside the introitus. Some however were less marked cases of descensus as the records indicate that the attending men in the service did not all have exactly the same idea as to the degree of descensus before the term prolapse should be used. Descensus of more moderate degree occasioned interference in 112 cases. Bleeding was the major indication in 53. In 50 cases in women past childbearing a symptom producing retrodisplacement was the reason for operation.

Nonmalignant bleeding whether caused by small myomas or by dysfunction, is in many cases, efficiently managed by vaginal hysterectomy. Both of these conditions are found for the most part in women who are nearing or who have reached the menopause and by far the greater number of them have had children. In many of them some outlet relaxation exists and a considerable number have cervixes which are not healthy. All of these conditions may be remedied by one procedure which has the added advantage of preserving the ovaries. Irradiation for the relief of nonmalignant bleeding in women in the early forties frequently causes much discomfort because of the menopause which appears rapidly as a result of the destructive effect of the irradiation upon the ovaries. The preservation of the ovaries permits the menopause to come much more gradually and the woman is far more comfortable than when the ovarian function is suddenly interrupted.

Larger myomas may be removed vaginally by excising the uterus piecemeal, or by morcellation. This is a procedure which demands a considerable degree of familiarity with the technique of the operation and which occupies a limited field. It should not be employed if an old subacute pelvic inflammation is present as the adhesions which this condition produces are extremely difficult to deal with from below. A simple form of morcellation in cases in which the uterus is not very large

but in which it is difficult to turn the corpus out anteriorly or posteriorly is the amputation of the cervix. This converts the uterus from a relatively pear-shaped mass into an irregularly round one. The latter can be turned out much more easily and with the exhibition of far less force.

In the treatment of marked descensus and of prolapse vaginal hysterectomy finds a place of real usefulness. In most of the cases of this country prolapse is managed either by the excision of the uterus with interposition of the broad ligaments or by some form of the Manchester operation. The removal of the uterus has been our preference and our experience with this procedure has been a very satisfactory one. The objection that the uterus in many of these cases is normal is of little weight. In most of these patients it has no further function. In the majority too, the cervix is not normal. It is lengthened, thickened, decubitus ulcers may be present, and the cervical canal is unhealthy. In the Manchester type of operation the cervix is usually removed. If the entire uterus is excised, not only the bases of the broad ligaments may be used for support but the upper portion as well may be utilized as a support for the bladder. In addition, if the uterus is removed the posterior herniation may be dealt with by uniting the uterosacral ligaments. This we have found to be one of the most important parts of the operation. The operation is nearly extraperitoneal and the patients, who in many cases are old women of deficient resistance, stand the operation very well. The tax upon the strength of the patient is far less than that which is caused by a plastic followed by an abdominal operation.

Women with symptom-producing retrodisplacement of the uterus, past the period of childbearing are often more efficiently managed by the removal of the uterus than by any one of the various retrodisplacement operations. In patients at this time of life it seems more logical to remove the uterus than to do a more prolonged procedure which is intended to secure it where it belongs. In many of these women there are associated lesions of the vagina and cervix which may with advantage to the patient, be cared for

at the same time Subtotal hysterectomy has been recommended for this condition, but we have, in a considerable number of cases, chosen to deal with it by vaginal removal of the uterus, with vaginal plastic at the same time In many of these cases the removal of a cervix which is often not normal is a further advantage Removal of the uterus by any method is not advocated for this condition in young women

Outlet relaxation together with a moderate descensus is a common finding in women in middle life Both of these conditions may be cured at one time by the vaginal removal of the uterus Small leiomyomas, endocervicitis, and menorrhagia are often present Discomfort caused by sagging or retrocession of the uterus is often seen, and these conditions are frequently accompanied by outlet relaxation and more or less abnormality of the cervix All of these may be corrected by one procedure with a minimal risk The pelvic discomfort in many cases is the result of varicose veins of the broad ligament and these are done away with by the hysterectomy

#### CONTRAINDICATIONS

Approach from below is contraindicated by a number of conditions When hysterectomy is indicated in the presence of extensive residues of pelvic inflammatory disease the excision is best performed abdominally The adhesions which may be found in these cases render the vaginal operation difficult and hazardous Previous pelvic operations may be followed by adhesions sufficiently extensive to render vaginal work difficult We have in a number of instances removed the uterus from below after some procedure for the shortening of the round ligaments had been done abdominally, but the operation has usually been difficult It should not be attempted unless the operator has had a considerable experience with vaginal surgery Patients upon whom suspension of the uterus to the abdominal wall for prolapse has been done are sometimes seen with the uterus again protruding This procedure has disappeared from gynecological clinics These patients may be operated upon from below, although it is sometimes difficult to bring the corpus of the uterus into the

vagina until the false ligament which has often formed between the abdominal wall and the fundus uteri is severed Access to this may be made much easier if an assistant presses down upon the lower abdominal wall Cases in which endometriosis is suspected are better approached from above as the dense adhesions characteristic of this condition are hard to manage from below Ovarian cysts, if not adherent, may be punctured and removed from below with no great difficulty, but the impossibility of being certain as to the exact character of the cyst before the abdomen is entered makes it wiser to treat them by abdominal incision

We do not recommend the operation for the treatment of carcinoma of the uterine corpus A very important early step in the performance of hysterectomy for corpus cancer is the blocking of the broad ligaments by placing straight 8 inch clamps alongside the uterus on either side to prevent the pushing out of cancer cells through the lymphatic vessels of the broad ligaments This may be done immediately when the approach is made from above When the operation is carried out from below the upper part of the broad ligaments is not occluded until late in the operation, while in the earlier stages the uterus will have been subjected to a considerable amount of handling In most of the cases of corpus carcinoma, it is technically possible to remove the uterus from below, but the impossibility of early closure of the broad ligaments interposes a serious objection to the employment of the operation

The technique of the operation used in our service has been described in a previous publication The usual vaginal hysterectomy done in cases other than prolapse may involve only the removal of the uterus, but in most of these cases some form of vaginal plastic is also done This may be only a perineal repair or an anterior plastic may also be necessary If urinary incontinence exists, it may easily be cared for when the hysterectomy is done The adnexa may be inspected through the vaginal wound

We have continued to employ the operation with ligature of all divided tissues, and have not been impressed by the clamp method of

removing the uterus. This operation, in the days of poor suture material and deficient asepsis, no doubt played a useful rôle. Today the completer surgical methods seem more satisfactory.

In the series of 517 vaginal hysterectomies here reported there has been no death. It must be conceded that there has been an element of good fortune in attaining so large a number without mortality. A well trained staff, proper selection of cases, and careful technique have played their part, but good luck has helped. It is scarcely likely that an other similar number may be done without the loss of a single patient. Although mortality has been absent, morbidity has not. It is not possible to do hysterectomy by any method without some morbidity, as a bacteria laden area is invaded whatever the type of operation chosen. The morbidity is somewhat higher in the vaginal operation than in either the total or the subtotal abdominal hysterectomy. By the standard of the American College of Surgeons, that is, a temperature of 100.4 degrees on any 2 days excluding the first, 42.1 per cent of our cases must be placed in the morbid group. In spite of this fact, convalescence has been as a rule smooth. The hospital stay in uncomplicated cases, is 11 or 12 days. Drainage is not used except in the cases of prolapse in which the dissection is rather wider than when the operation is done for other reasons. In cases in which the uterus protrudes from the introitus and the broad ligaments are interposed between the bladder and anterior vaginal wall with the freed pubo-cervical fascia as an additional support a small drain of rubber tissue is placed in the wound at the vaginal vault and is removed in 24 hours.

There were some more serious sequelae. Postoperative bleeding occurred in 15 cases. In all the cases in which bleeding occurred during recovery it was easily controlled by a clamp or suture at the vaginal vault. In no case did a notable loss of blood occur. Pelvic abscess required opening in 7 cases. A vesical injury occurred in 3 cases. In 2 of these after immediate repair an uneventful convalescence followed. In 1 urinary extravasation caused some trouble but the patient recovered. In 1 case a small nick in the rectum was

made while doing a perineal plastic after the hysterectomy but suture was followed in a smooth recovery. One old woman, after an operation for prolapse had a cerebral hemorrhage on the 10th day but recovered.

A common criticism of the operation is that it shortens the vagina. This, in our experience has not occurred except in those cases in which the operation is done for extreme descensus. In these cases the anterior and posterior vaginal walls have been everted with the uterus and shortening has already taken place. In cases in which the uterus is at its normal level, or in which descensus is moderate a vagina of normal depth may be left. When the uterus is totally excised, whether it is done abdominally or vaginally if the vaginal wall is divided close to the cervix there will be no shortening or the difference in length will be so small that it will not be noticed. This has been true in so large a series of total hysterectomies by both methods that the fact appears to be definitely established.

Many of the technical difficulties of which some operators complain are due to the use of improper instruments. Bulky retractors and clamps not designed for use in this field take up so much of the limited space that work is impeded. Narrow curved retractors, fitting the bodily curves and occupying but little space in the field are extremely useful. Proper clamps with rather shorter jaws than those used in the abdomen, and with a gentle curve, add to the ease with which hysterectomies other than those done for prolapse are carried out. It is wise to replace each clamp with a suture ligature immediately. This leaves the operative field free of dangling instruments which are in the way and is much more efficient from the standpoint of hemostasis. A small laparotomy pad, about 5 inches square always with a tape attached, is useful after the uterus is out and while the remaining clamps are being replaced by sutures. Unmarked gauze should never be placed in the vaginal wound. Heavy catgut is unnecessary. No. 1 chromic gut is sufficiently heavy for the major ligatures and sutures and plain No. 1 or No. 0 for all others.

In many of our cases cystocele and rectocele have been dealt with, and in a large

umber the perineum has been restored. When the patient is a nullipara, or if the perineum has been previously repaired, a small median episiotomy helps by giving greater exposure. This can be closed by sutures at the close of the operation.

While vaginal hysterectomy after previous pelvic surgery is, as a rule, inadvisable, we have, in a number of cases, removed the uterus from below after a laparotomy had been done. In nearly all these cases the previous operation had been for retrodisplacement or descensus. Vaginal hysterectomy after a retrodisplacement operation may be quite difficult, especially in the identification of the anterior peritoneal fold. In such cases the operator may solve the problem and keep out of danger by delivering the uterus posteriorly without having opened the anterior peritoneal fold, and, after having brought the corpus out, pass the finger up behind the uterus until the anterior fold is identified. It may then be opened without endangering the bladder. If the operation is done after a previous suspension for descensus a long false ligament between the fundus of the uterus and the anterior abdominal wall may cause some difficulty, although it may usually be reached and divided after the broad ligaments have been dealt with. In 1 case, because the true state of affairs inside the abdomen was not realized, the fundus was found firmly adherent over a considerable area to the anterior abdominal wall. The uterus could not be delivered. The fundal attachment was finally divided with difficulty, a thin layer of uterine tissue being left attached to the wall of the abdomen. This description merely indicates what may be done, but not what is advisable. When in doubt as to the state of affairs within the pelvis, it is best to make the attack from above.

One of our staff is studying the effect of the insufflation of a mixture of sulfanilamide and

sulfathiazole into the vaginal wound as it is closed at the end of the operation. This mixture is blown into the space between the peritoneum and vaginal wall and upon the vaginal vault after closure. The result of this work will be reported later. The peritoneal invasion is limited in its area, and painstaking vaginal preparation before operation decreases the likelihood of introducing infection. The use of the sulfonamides may still further reduce this likelihood.

#### SUMMARY AND CONCLUSIONS

This series includes all cases done during a stated period by all the members of the department of gynecology and obstetrics of the Evanston Hospital, including the younger men of less experience. The operation properly carried out appears to be a very safe procedure and one which is followed, in most cases, by a rather smooth recovery. There is a definite morbidity which in nearly all cases is not severe. A few patients required attention to abscesses or bleeding. None of these presented a serious problem.

The operation has a definite value and should find a wider employment than it does. It has limitations which should be observed. Those who have had limited experience with it should select the easier cases for attack from below. With adequate experience many patients may be dealt with vaginally without difficulty. It is not wise to regard this procedure as one which may be used routinely or even in too great a proportion of all cases. With proper selection of cases and with an adequate technique it is an extremely useful addition to operative resources. The pelvic surgeon should be sufficiently master of the various methods of removing the uterus that his choice of procedure may be based wholly upon the conditions presented in each case. It should not be influenced by lack of familiarity with any one of the available methods.



# EXPERIMENTAL PRODUCTION OF BRONCHIAL FISTULA IN RATS AND RABBITS

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THE purpose of this research was to provide a means by which carcinogenic substances could be applied directly to the bronchial mucosa of rabbits and rats in an attempt to produce bronchogenic carcinoma. Many methods have been used in the past to produce lung tumors in susceptible animals. Carcinogens have been rubbed on the skin (3) and have been injected intravenously (5) subcutaneously (2) and intratracheally (6). They have been applied on threads which have been threaded through the chest cavity (2). Susceptible animals have been subjected to atmosphere laden with dusts (4). The results of these methods were largely the production of lung tumors which seemed to arise from alveoli and were predominantly subpleural in distribution. They contained few mitoses and showed slight or no tendency to metastases. More important, they had no relations to the bronchioles and were not true bronchogenic tumors.

It was our thought that if we could produce a permanent bronchial fistula in animals which were susceptible to induced tumors, we could possibly produce a more typical lung tumor by repeated application of carcinogenic substances directly to the bronchial mucosa. Adams and Livingstone in 1931 described a method for the production of bronchial fistulas in dogs. With several modifications this principle was found applicable to rats and rabbits.

## METHOD IN RATS

Adult white rats were used in these experiments and ether anesthesia was administered through a loosely fitting face mask. The left chest was used routinely because only one large lung lobe is present on this side in rats. This made the procedure easier, more uniform,

and above all the resulting fistulas were better and easier to keep open.

At the beginning a two stage procedure was used. The chest wall was opened through the left 5th interspace and the lung lobe brought out through the incision. Pericostal sutures were then placed on either side of the lobe and the ribs brought together fairly tightly over the exteriorized lung. The muscles and skin were then brought together over the lobe thus completing the first stage. The second stage was performed 5 to 10 days later in order to give time for healing and fibrosis to take place between the lung tissue and the chest wall. The wound was then reopened and the lobe cut off a short distance from the chest wall. The bronchus was identified by probing and a foreign body inserted to keep it open. The skin was sutured to the underlying muscle and the wound was left wide open.

The method mentioned of producing bronchial fistulas was found to be unsatisfactory yielding only 25 to 50 per cent desired results for the following reasons. There was no way to determine accurately the tension on the pericostal sutures and they were frequently either too tight or too loose. When they were too tight the lung tissue would completely slough before the second stage and when they were too loose, the lobe would either slip back into the chest cavity or marked bleeding would take place when the lobe was cut off. This bleeding was very troublesome because even if we did manage to stop it before the animal died, we would frequently have the main bronchus also tied off because of its very close proximity to the main vessels.

These problems were solved by performing the whole operation in one stage. The lung lobe was brought out through the 5th interspace and the pericostal sutures were placed as mentioned. Then the lobe was immediately cut off a short distance from the chest wall. No bleeding occurred if the stitches

From the Department of Surgery, The University of Chicago.  
This work has been conducted under grant from the Douglas  
Smith Foundation for Medical Research of The University of  
Chicago.

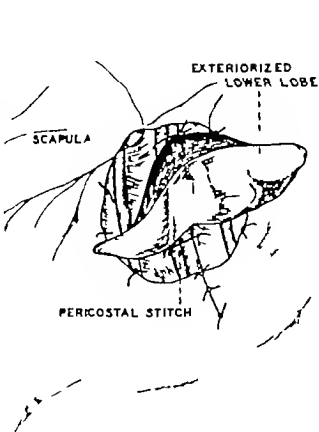


Fig 1

Fig 1. The lung lobe is exteriorized and the adjacent ribs are brought together about the hilus

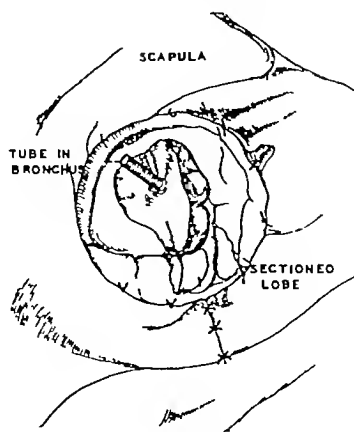


Fig 2

Fig 2. The exteriorized lung lobe has been cut off and a

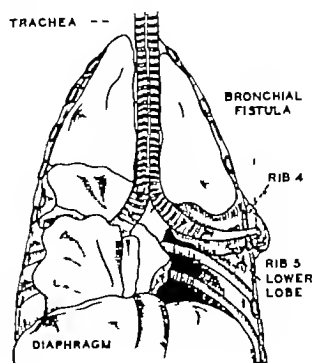


Fig 3

foreign body has been inserted into the bronchus

Fig 3. A ventral section through the chest of a rabbit to show the relations of the trachea, bronchus, and fistula

were reasonably tight. The bronchus was then identified and a short piece of twine was inserted. The wound was then closed about the twine and one suture was taken through the twine and the skin as a means for keeping it immobile. About 5 days later when the twine could be removed, a fistulous tract was left which was wide open and quite straight.

Eighteen rats were operated upon by the method described. Three died at operation apparently from too much ether. Two died of tracheal obstruction caused by the twine slipping inward. Three did not develop fistulas because the twine slipped out. Ten rats developed large fistulas demonstrable by x-ray with iodized oil injection.

Before we were able to obtain uniformly good results two major problems presented themselves. The first was to get the animals to survive the open pneumothorax. In rat operations, speed and dexterity proved to be the answer. Immediately after the pleural cavity was opened the pericostal sutures were placed. The chest wall was kept closed at all times by the assistant, except while the lung lobe was being brought out. After first few operations it was rare to have a rat die on the operating board from open pneumothorax.

The second problem involved the material to be used to keep the bronchus open. Rubber and metal tubes and cotton and gauze packing were tried but none would stay in place long

enough to give the superficial tissues time to heal. We finally tried ordinary wrapping twine (about 10 turns to inch) which solved the problem. Because this twine swells when it absorbs moisture, it stayed in place and kept the bronchus dilated while the wound healed.

#### METHOD IN RABBITS

The principle of the production of bronchial fistulas in rabbits was the same as that in the rats and only differences in technique will be elaborated.

Rabbits have much less resistance to infection than do rats, therefore it was necessary to perform operations with more attention to sterile technique. In spite of this precaution, many rabbits died with a profuse pleural infection, developed either at or after operation.

Because rabbit lungs were found to be more friable and more difficult to bring out of the chest cavity, some method other than speed had to be developed to combat the pneumothorax. A positive pressure ether apparatus was devised which proved adequate. The positive pressure was not applied until the rabbit was deeply anesthetized because otherwise laryngeal spasm forced the ether mixture into the stomach. With this apparatus we were able to keep rabbits alive with open chests for as long as 1 hour.

Specially made brass plugs were found to be the best means for keeping bronchi open



Fig. 4. X-ray film with iodized oil showing bronchial fistula in rat.

They were pointed and grooved at one end to facilitate introduction into the bronchus.

It was also found advisable to immobilize the rabbits forelegs during the first 6 to 8 postoperative days because their scapulas and elbows were constantly disturbing the operative field. For this purpose gauze soaked in starch was used to good advantage.

Operations were performed on 24 rabbits by the technique described. Eight died at operation either from too much ether or from a lack of air exchange. Six died after operation from profuse chest infections. Ten developed open bronchial fistulas demonstrated by x ray with iodized oil injection.

Both rats and rabbits with bronchial fistulas require constant attention in order to keep the fistulas open. If they are left alone without twine or tube in place the fistulas heal spontaneously within a very short time.

While these experiments were going on, and also at the present time these fistulas were being treated with carcinogenic substances notably benzpyrene. Applications were made every other day for as long as 3 months with no definite gross evidence of cancer being found.

In addition studies are being carried out on the effect of exteriorization *per se* on lung tissue. These are not complete enough to report at the present time, but indications are that some metaplasia of bronchial mucosa takes place in addition to the production of fibrosis and atelectasis.



Fig. 5. X-ray film similar to that in Figure 4, showing bronchial fistula in rabbit.

#### SUMMARY

1. Production of persistent bronchial fistulas in rats and rabbits is deemed worthwhile because of the possibility of inducing the bronchogenic tumors by direct application of carcinogens to the bronchial mucosa.

2. Procedures are described for the experimental production of persistent bronchial fistulas in rabbits and rats.

3. Results of treatment of bronchial anocyst directly through the fistula with the carcinogen benzpyrene for a period of 3 months are grossly negative.

4. The possibility that lung tissue is changed morphologically by exteriorization *per se* is mentioned and is being studied further.

#### REFERENCES

1. Adams, W. E. and LITTMAN, H. M. *Surg. Gyn. Obstet.* 91: 53, 479.
2. AUSTIN, J. F. B. *Pub. Health Rep. Wash. D. C.* 5: 534.
3. SUGARMAN, M. *Am. J. Cancer* 44: 39, 65.
4. SUGARMAN, M. G. and BENSON, E. L. *Am. J. Cancer* 49: 18, 65.
5. SUGARMAN, M. B. *Arch. Path.* 62: 39, 77, 82.
6. Idem. *Am. J. Cancer* 39: 51, 517-522.

# BENIGN TUMORS OF THE LARGE INTESTINE—

## Incidence and Distribution

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A COMPARISON of the published reports dealing with the incidence and occurrence of benign tumors of the large intestine shows a marked discrepancy in the prevalence of these tumors. This discrepancy may be accounted for in a number of different ways. Thus if the specimens for study have been removed at surgical operation only those tumors which have produced symptoms are likely to be included. If the material for study is obtained from autopsies the incidence will vary with the care taken to note the presence of the tumors. And, finally, when the incidence of tumors is determined upon the basis of a small series of cases, the results are less likely to be reliable.

The term polyp is commonly used to designate any benign tumor either sessile or pedunculated arising from the mucous membrane of the large intestine. While this interpretation of the term polyp may convey the gross conception of the tumor, it does not signify the essential pathological structure of the tumor. On the basis of the exact structure, this group of tumors referred to grossly as polyps may be classified into a number of different types such as adenomas, leiomyomas, carcinoids, and lipomas. Since each type of tumor is characterized by a distinct clinical course and prognosis the necessity of an accurate diagnosis is obvious. The explicit nature of the polyp must be known in order to arrive at the correct treatment and prognosis. In this study of the large intestine, the occurrence and exact nature of each polyp was determined.

### MATERIALS AND METHODS

This report is based upon 1,460 consecutive autopsies in which the entire large intestine was available for study. Each intestine was carefully examined in the fresh state. All

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grossly discernible elevations and irregularities of the mucosa were recorded and the distance of each was measured from an anatomical landmark. Each elevation, together with the adjacent intestinal wall, was removed and placed in 10 per cent formalin. After fixation, sketches of each lesion and the pertinent descriptive information were recorded on an anatomical drawing of the large intestine. Large lesions were sectioned in a plane perpendicular to the mucosa. All blocks of tissue were then embedded in paraffin in such a manner that the plane of section was at a right angle to the plane of the mucosa. Single sections and in many instances step and serial sections were prepared and stained with hematoxylin and eosin. The microscopic appearance of the lesion was then noted and studied in relation to the gross appearance. On the basis of the microscopic structure, the exact diagnosis of the lesion was established. All carcinomas and sarcomas have been excluded from this study, although a small number of adenomas showing microscopic foci of carcinoma have been included. The adenomas containing foci of carcinoma will be discussed in detail in another communication. Also all lesions obviously the result of inflammation, thrombosed hemorrhoids, and anal fibrous tags have been excluded.

### TYPES OF POLYPS

The number of cases and the various types of polyps encountered in the large intestine in this series are as follows:

Adenoma, 139, lipoma, 13, carcinoid, 1, leiomyoma, 1, a total of 154 cases.

*Adenomas.* In the 1,460 consecutive large intestines studied there were 139 which contained adenomas, an incidence of 9.5 per cent. Omitting one instance of familial polyposis, the remaining 138 contained a total of 272 adenomas. In 80 instances there were single adenomas and in 59 cases 2 or more adenomas



Fig. left Adenoma of the sessile type.  $\times 36$   
 Fig. right Adenoma of the pedunculated type. The stalk is covered with normal mucosa.  $\times$

were present. Table I shows the incidence of adenomas in the colon and rectum.

TABLE I—INCIDENCE OF ADENOMAS IN COLON AND RECTUM

	Adenomas solely in one site		Adenomas present in both sites		Total	
	Cases	Per cent	Cases	Per cent	Cases	Per cent
Colon	3	7.5	7	5	10	8
Rectum	8	20	7	5	15	20

In this series the incidence of adenomas in the colon, 8.22 per cent, was appreciably greater than that reported by others. Stewart found 4.9 per cent in 1815 autopsies, Susman 6 per cent in 1100 autopsies, and Lawrence only 2.37 per cent in 7,000 autopsies. Lawrence attributed the low incidence in his series to the large number of children included, 25 per cent of the 7,000 autopsies being on children under 11 years of age. However, in the present study the percentage of autopsies of children less than 11 years of age was also 25 per cent. In the 460 autopsies the incidence of adenomas in the rectum was 2.39 per cent compared with the observation made by Lawrence of 0.42 per cent. In both series approximately one-half of the intestines with adenomas in the rectum also showed adenomas in the colon. In the present series the number of adenomas noted in the rectum was about five times the number recorded by Lawrence, and the number of adenomas of the colon was three times the figure reported by the same author. However, in general the relative incidence of adenomas in the

rectum and colon was in agreement with the observation of Lawrence and in disagreement with the experience of Swinton and Warren. The identification of the adenomas studied by Swinton and Warren was dependent largely on roentgenographic and proctoscopic examinations. These workers were able to visualize 70 per cent of the tumors in their series through a 10 inch sigmoidoscope. Obviously the greatest number of adenomas would be encountered in that segment of the large intestine in which the sigmoidoscope is applicable. It would appear doubtful that the highly selected material could give the true incidence of adenomas of the rectum and colon.

Table II shows the distribution of the adenomas.

TABLE II—DISTRIBUTION OF ADENOMAS

	Cases	Per cent
Cecum	17	11.1
Ascending colon	41	
Hepatic flexure		6.4
Transverse colon	3	1.9
Splenic flexure	1	
Descending colon	12	
Sigmoid colon	76	
Rectum	43	11.1
Total	172	

From Table II it is seen that the sigmoid colon is the most common site in the large intestine for the occurrence of adenomas, 27.4 per cent occurring in this segment. It was found 20 of 51 polyps located in the sigmoid



Fig 3

Fig 4

Fig 5

Fig 3 Photomicrograph of the adenoma shown in Figure 1 Note variation in type of cells lining glands  $\times 85$

Fig 4 Photomicrograph of a section through the periphery of the adenoma which is shown in Figure 2 The

cells are tall, columnar and contain mucus  $\times 85$

Fig 5 Photomicrograph of the base of the adenoma shown in Figure 2 The cells lining the glands are columnar but do not contain mucus  $\times 85$

colon, although it is not clear that all of the tumors were adenomas. In an analysis of 166 cases of adenomas of the colon, Lawrence found the sigmoid colon involved 43 times. In an additional 13 cases the sigmoid colon was involved as part of a generalized polyposis of the colon. The observations in the present study are in agreement with the experiences of Saint and of Lawrence, that the sigmoid colon is the most commonly involved site.

The adenomas may be either sessile (Fig 1) or pedunculated (Fig 2). A few were as small as 1 millimeter in diameter and the largest measured 9 centimeters in the greatest diameter. Numerous adenomas studied in the one case of multiple polyposis involving the entire colon and rectum in this series were similar in all characteristics to the solitary and multiple adenomas in the other cases.

Histological studies of the adenomas revealed a variable structural and cytological picture. The supporting framework ranged from a single, simple connective tissue stalk to multiple complex branching cores of connective tissue. In some instances the muscularis mucosae extended upward from the wall of the intestine into the pedicle, and in others only isolated foci of smooth muscle were noted in the stalk. The stalks contained a variable but usually moderate number of small and

large blood vessels. The normal mucosa of the intestine either terminated at the base of the adenoma or, particularly if the polyp was of the pedunculated type, covered the base and stalk. Regularly arranged columnar epithelium disposed in the form of glands covered the connective tissue stalks. The glands varied in size and contour. The columnar epithelium ranged from cells with pale acidophilic cytoplasm to cells of the goblet type with clear cytoplasm. In some instances an entire adenoma showed a single type of cell and in other examples a single polyp exhibited variations of cell type (Fig 3, 4, 5). Thus one adenoma would be comprised entirely of mucus-filled cells whereas another would exhibit only a few, if any, cells of this type. Mitotic figures were encountered frequently in some adenomas and were uncommon in others. From the aforementioned description it is apparent that not only was there variation among different adenomas but that a single or solitary adenoma frequently exhibited a pronounced variation in structure.

**Lipomas.** The lipomas constitute the second most frequent group of polyps found in the large intestine. In the 1,460 consecutive large intestines observed in the present series, 13 contained lipomas, an incidence of 0.89 per cent. Comfort found 20 submucous intestinal lipomas in 3,924 consecutive autopsies.

Fig. 6. Lipoma of the pedunculated type.  $\times 5$ Fig. 7. Lipoma of the sessile type.  $\times 44$ 

gies. Two of these were located in the large intestine an incidence of 0.25 per cent. Staemmler noted only 9 cases of lipomas of the entire intestinal tract in 17 000 autopsies, an incidence of 0.05 per cent. The greater incidence recorded in the present series is probably the result of a more careful examination.

In the present group of 13 large intestines, 10 showed a solitary lipoma and 3 contained 2 or more. Of the 3 instances of multiple lipomas the cecum and ascending colon were involved in 1 instance, the ascending colon and sigmoid in another, and only the cecum in the third. The distribution of the lipomas was as follows:

Of a total of 20 cases the lipomas were in the cecum in 9 cases, in the ascending colon in 8 cases, in the descending colon, sigmoid colon, and rectum in 1 case each, while none was found in the hepatic flexure, transverse colon, or splenic flexure.

The cecum and the contiguous ascending colon are the most common sites of lipomas in the large intestine. This result is in agreement with the conclusion of Comfort and contrary to the observations of Stetten. Stetten, analyzing cases from the literature, found the predominant site of lipomas to be the sigmoid colon and rectum. Both the sigmoid colon and rectum were involved more frequently than either the cecum or ascending colon. In the analysis made by Stetten the presence of some of the tumors was noted because of clinical symptoms. Since the rectum and sigmoid colon are accessible for direct examination, the identification of the tumors in these locations was probably more readily established.

The distribution according to sex showed 4 men and 9 women, although the ratio of male to female autopsies was about 3 to 1. Comfort, analyzing the reported lipomas of the entire gastrointestinal tract, noted the cases about equally divided between the two sexes.

TABLE III.—OCCURRENCE OF LIPOMAS

Age group	Submucosa	Subserosa
Under 30 years	85†	
30 to 40	33	1
40 to 50	200	1
50 to 60	191	

Table III shows the age of the patients in whom the lipomas were encountered. With the exception of one patient, a man 31 years of age, all were over 50 years of age. Thus the incidence of lipomas is greatest in the same decades in which adenomas and carcinomas are most common.

The lipomas of the intestine may occur in either the submucosa or the subserosa or more rarely involve both sites. In the present study of 13 cases the submucosa was the site involved in 12. In the other case the tumor was located in the subserosa of the sigmoid colon but produced an elevation of the mucosal surface. Incidentally this was the only lipoma of the large intestine found in a patient under 50 years of age.

Two of the large intestines containing lipomas also contained adenomas. Furthermore 2 other large intestines with lipomas presented a carcinoma. Thus in 4 of the 13 cases of lipoma there was another type of tumor involving the large intestine. This fact may signify a special susceptibility in these patients to the development of tumors.

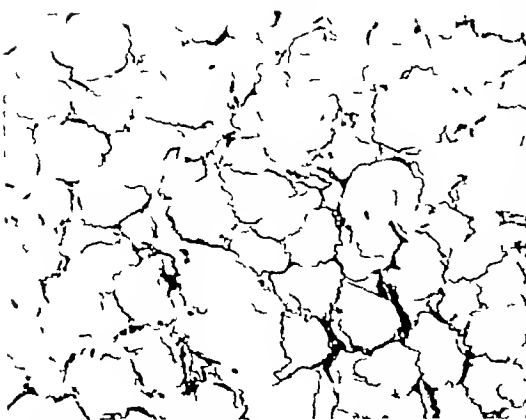


Fig 8 High power photomicrograph of the lipoma shown in Figure 7. The fat cells are of the adult type.  $\times 100$

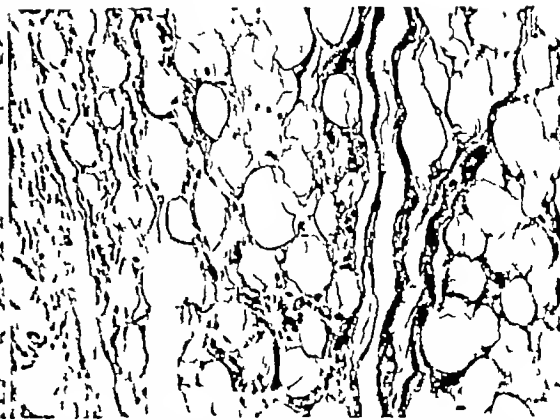


Fig 9 High power photomicrograph of the lipoma shown in Figure 6. Some of the cells are cuboidal and fusiform with a granular and vesicular cytoplasm.  $\times 100$

In 3 of the 12 cases of submucosal lipomas there were single pedunculated tumors (Fig 6). The lipomas of the 9 other cases were sessile (Fig 7). Grossly the tumors were soft, smooth, and pale gray or grayish-yellow. The pedunculated lipomas were attached to the wall by narrow flat stalks. These tumors were oval in shape and flattened in one dimension.

Histologically the tumors were comprised of the adult type of fat cell (Fig 8). The fat cells were arranged in groups of variable size which were separated by irregular connective tissue trabeculae. The trabeculae were usually delicate, but in a few instances the connective tissue was relatively abundant. Blood vessels,

usually small, were dispersed throughout the septa. Peripherally, the lipomas were surrounded by a thin but variable zone of connective tissue. Occasionally this layer of connective tissue was poorly defined. Although Staemmler described an immature type of fat cell at the periphery, none was noted in this location in this series. However, within some of the lipomas cuboidal or fusiform cells with a granular and vesicular cytoplasm were noted (Fig 9). Except for scanty collections of lymphocytes there was no infiltration of inflammatory cells, although a few lymphoid nodules were sometimes present at the level of the muscularis mucosae. Thus these lipomas

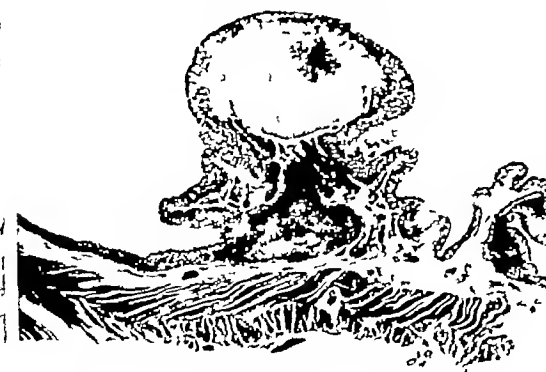


Fig 10 Leiomyoma of the pedunculated type. The tumor is separated from the muscularis by a stalk of connective tissue.  $\times 36$

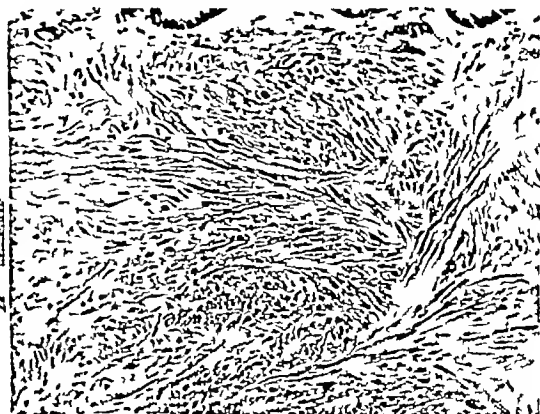


Fig 11 Section of leiomyoma shown in Figure 10. The tumor is composed of interlacing bands of smooth muscle cells, and is continuous with muscularis mucosae.  $\times 110$





Fig. 3. left. Carcinoid of the rectum. Not the intact layer of mucosa.  $\times 3$ .  
 Fig. 3. Photomicrograph of the carcinoma shown in figure 3. The cells are arranged in cords and in alveolar structures.  $\times 6$ .

have not produced evidence for the origin of the tumors on an inflammatory basis. In the smaller tumors there was no disturbance of the muscularis. In the larger lipomas, the muscularis was slightly compressed and distorted by the tumor. The muscularis mucosae varied from a well defined layer to only thin remnants. The tumors in all instances were covered on the lumen surface by mucosa. The most outstanding change of the mucosa was an attenuation of the glands and decrease in the width of this layer. The goblet cells in some instances were prominent but for the most part were not noticeably changed. In a few instances the capillaries of the mucosa were distinctly dilated and hyperemic.

The clinical diagnosis of a lipoma of the intestine frequently rests upon the presence of a complication such as obstruction in tumescence or spontaneous expulsion. If only those cases which have produced obvious clinical signs are recorded the incidence of lipomas of the colon would appear abnormally low. This study based on autopsy material indicates that the actual incidence is much greater. Many lipomas of the large intestine probably never produce manifest clinical symptoms.

**Leiomyoma.** Only one tumor composed of smooth muscle was encountered in this series of 1,460 autopsies. It was located in the sig-

moid colon of a 67 year old man and formed a pedunculated firm mass measuring 11 centimeters in the greatest diameter (Fig. 10). Its mucosal surface was smooth and reddish-brown. Histologically the tumor was composed of elongated smooth muscle cells with a tendency to be arranged in interlacing bands (Fig. 11). A few small blood vessels were present within the tumor. No mitotic forms or giant cells were noted. The tumor was poorly delineated from the muscularis mucosae and was not encapsulated. Golden and Stout have pointed out that the lack of a capsule of the intestinal leiomyoma may be used in differentiating this tumor from smooth muscle sheath tumors. The stalk consisted of connective tissue within which were several small and large blood vessels. There was no connection between the muscularis and the tumor. The pedicle and most of the tumor were covered by an essentially normal mucosa. One segment of the mucosa surrounding the tumor showed fibrosis of the stroma. This area might possibly represent a focus of inflammation. The indefinite demarcation of the tumor from the muscularis mucosae suggested that the latter was the point of origin.

Leiomyomas of the large intestine are uncommon. Golden and Stout did not encounter a single leiomyoma of the large intestine in

5,869 autopsies although 8 cases were garnered from specimens obtained from surgical operation. However, such material does not form a reliable index of the true incidence of disease processes. Comfort, probably referring to the entire gastrointestinal tract, stated that lipomas occur in approximately the same frequency as myomas. In the present study of large intestines the lipomas were much more common than the leiomyomas.

Golden and Stout have recently made a comprehensive analysis of leiomyomas of the gastrointestinal tract which have been reported in the literature. In addition to the submucosal location of the tumor as described in this report the tumors may be subserosal, intramural or combined subserosal and submucosal.

*Carcinoid* The fourth type of polyp encountered in this series was the carcinoid or argentaffinoma. The carcinoid occurs most commonly in the appendix and less frequently in the ileum. As determined by the reports in the literature it is a decidedly uncommon tumor of the large intestine. Ashworth and Wallace, in a review of unusual locations of carcinoid tumors, found 11 cases in addition to 1 of their own in which the tumor was located in either the colon or rectum. Two tumors were located in the cecum, 2 in the sigmoid colon and 2 in unspecified sites. The 5 remaining tumors were situated in the rectum.

In the present report the tumor was located in the rectum of a man 56 years old. Grossly the tumor formed a firm hemispherical elevation measuring 15 millimeters in the greatest diameter, which projected into the lumen of the intestine (Fig 12). A smooth but otherwise normal-appearing mucosa covered the nodule. The entire nodule moved freely with the submucosa, but the mucosa was closely affixed to the tumor. The cut surface of the tumor was grayish yellow.

Histologically the layer of mucosa was thin but intact. The muscularis mucosae formed a generally distinct but thin layer beneath the mucosa. There were lymphoid nodules centered at this level. Bounded by the muscularis mucosae and occupying the submucosa was a nonencapsulated nodule of tumor (Fig

13). The cells of the tumor were arranged in nests and more frequently in cords, which often exhibited a disposition to intercommunicate and form alveolar structures and pseudorosettes. The cells were either polygonal or cylindrical and the cytoplasm, pale and acidophilic. The nuclei were either round or oval and contained a moderate number of fairly evenly distributed chromatin granules. No mitotic figures were noted. When the cells were cylindrical and arranged in columns, the polarity of the nuclei within the cells varied but the shape and size of the nuclei were remarkably uniform. The nests and columns of cells were separated by a stroma of connective tissue which ranged from fine septa to large dense bands. Small blood vessels were present within the stroma. A few collections of tumor cells were noted within the muscularis mucosae. The base of the nodule showed nests of tumor cells extending irregularly into the submucosa. However, this layer was greatly thickened so that a wide zone of connective tissue uninvolved by tumor existed between the nodule and the muscularis. Within this connective tissue were numerous small and large vessels. The muscularis underlying the tumor nodule was slightly thickened. One section on microscopic examination disclosed a small focus of tumor unconnected with the main nodule lying immediately external to the muscularis. No other foci of tumor were discernible. Although early investigators (3, 6) regarded the carcinoid as a benign tumor, more recent workers (8, 9) have recognized the malignant character of some of these tumors. Raiford has stated that carcinoids situated in the stomach or colon are more likely to be malignant. The tumor described in this report probably should be regarded as malignant since a small nest of cells was encountered external to the muscularis. However, the cytological features did not differ in any way from those of a benign carcinoid.

Although Wyatt stated that carcinoids do not occur in the rectum, 6 cases including the present one have now been reported in this location.

The generally accepted opinion is that the carcinoid is derived from the Kultschitzky

cells of the mucosa of the intestine. Since Pessan has described these cells as occurring occasionally in the large intestine carcinoid tumors might be expected to occur in this location. It is entirely possible that in some instances the carcinoid tumor has been confused with the carcinoma in this particular location.

#### CONCLUSIONS

1. The adenoma is the most common polyp of the large intestine.
2. The most frequent site of the occurrence of adenoma in the large intestine is the sigmoid colon.
3. The second most frequent polyp of the large intestine is the lipoma.
4. The most common sites in the large intestine of the lipoma are the cecum and ascending colon.
5. The leiomyoma is an uncommon tumor of the large intestine.

6. Carcinoids of the large intestine are frequent. A carcinoid of the rectum is recorded.

#### REFERENCES

1. ARNOLD, C. T. and WALLACE, S. A. *Arch. Path. Ch.*, 64, 1, 27.
2. CONNOR, M. W. *Surg. Gy. Obst.*, 1917, 25, 38.
3. FORBES, W. D. *Bull. Johns Hopkins Hosp.*, 37, 30.
4. GOLDEN, T. and STORY, A. P. *Surg. Gyn. Obs.*, 64, 73, 764.
5. LA. MINCE, J. C. *Ann. J. Surg.*, 1926, 51, 420.
6. OBER DOUGER, S. *Friedl. Zsch. Path.*, 1911, 1.
7. PESSAN, S. B. *Arch. Path. Ch.*, 1921.
8. PORTER, J. E. and WHILLAN, C. S. *Am. J. Cr.*, 1930, 36, 343.
9. RUPPEN, T. S. *Am. J. Cancer*, 1922, 18, 93.
10. SALL, J. H. *Bull. J. Surg.*, 1927, 5, 60.
11. S. AFRINGER, M. *Des. Lipom. Le. Enkel. et. Blasenblut. Des Neubildungen des Darmes*, 1924, pp. 273-279. Stuttgart, 1924.
12. STETTER, D. *Surg. Gyn. Obst.*, 1900, 9, 36.
13. STYRKE, M. J. *Lancet*, Lond. 191, 604.
14. S. SM. W. J. *Path. Bact. Lond.*, 1921, 11, 76.
15. SWITZER, A. W. and HARRIS, S. J. *Am. M. J.*, 1930, 3, 927.
16. W. T. T. E. *Ann. Surg.*, 1938, 107, 704.



being used. The wound itself is cleansed with sterile sponges or cotton pledgets wet with sterile normal saline solution. The whole area is scrubbed for 20 minutes by the clock, the solution of soap and water being changed several times during the process. The skin may be prepared further with ether and tincture of mercuric or merthiolate. No antiseptic is used in the wound. This procedure is carried out by the surgeon or his assistant. Only thoroughly trained personnel should be entrusted with its responsibility.

After the wound is draped with sterile sheets it is irrigated with 1000 cubic centimeters of normal saline followed by 500 cubic centimeters of a saturated solution of carbamide sulfonamide mixture in sterile water. Asepto syringes or an overhead tank with rubber tubing and a glass nozzle are used for this purpose.

Careful and thorough débridement of the wound is then carried out under strict aseptic conditions. The procedure consists of excising about  $\frac{1}{4}$  to  $\frac{1}{2}$  of an inch of skin around the edges of the wound and removal of all necrotic or injured fat, muscle, or fascia. The amount of tissue taken out is determined by its color, ability to bleed, contractibility of muscle and general appearance (16). Loose fragments of contaminated bone and periosteum are removed. Those pieces of clean bone attached to periosteum may be left *in situ*. During débridement, and other preparation of the wound, a minimum of suture material is used, plain catgut serving for bleeders. The débridement can be described as a partial excision or saucerization of the wound. Irrigation is then repeated with first a normal saline and then a saturated carbamide sulfonamide mixture solution.

Reduction of the fracture is accomplished by traction. When indicated a bone plate may be employed, the fracture impacted, and the bone screws tightened. Lacerated tendons are approximated, the edges are freshened and by means of silk sutures are then brought together after the method of Bunnell.

The surgical procedure proper having been completed, about 1 to 6 ounces of carbamide sulfonamide mixture powder is sprinkled and packed into every part of the wound the

quantity used depending upon the extent of the lesion. It is important that no area be overlooked. The handle of a Band-Packer knife, a spoon, or a curette may be used to implant the powder. No attempt is made to close the various layers of the wound. The skin alone is approximated by means of a perpendicular mattress suture of silk.

Immobilization is achieved by either internal fixation or the application of a plaster of Paris cast. Since all soldiers have had tetanotoxoid a booster dose of 1 cubic centimeter is routinely given. In some of the more severe injuries a prophylactic injection of 5-1200 units of gas antitoxin may be administered intramuscularly. Sulfathiazole or sulfanilamide may be given orally for the next 7 days. Some of our patients were given sulfathiazole and some sulfathiazole; however the latter seems more satisfactory in maintaining an effective blood sulfonamide level. Blood sulfonamide determinations, red and white cell differentials, counts, and urine examinations are made on alternate days. Unless there is evidence of spreading infection the wound is left alone and is not inspected until the 7th to the 10th day. Skin sutures are removed after the 10th postoperative day.

#### COMPOUND FRACTURES RESULTING FROM ORDINARY TRAUMA

Table I illustrates the results of treatment in various types of compound fractures and severe tendon injuries encountered in civilian practice that is trauma resulting from automobile accidents, athletics, fighting, etc. The interval between the injury and treatment varied from  $\frac{1}{4}$  to 12 hours. All were treated by scrubbing, irrigation, débridement, irrigation, reduction, insertion of carbamide sulfonamide mixture powder and primary closure as has been described. Sixteen wounds healed *per primam* and the 2 others healed with a slight serous discharge but no gross infection. In both of the latter instances the skin was approximated under tension. It is interesting to note that in Case 1 patient incurred his injury while riding a scooter in a barnyard. His wound was contaminated with manure. Healing however occurred without infection. The following case Case 2 may be described

TABLE I—COMPOUND FRACTURES FROM ORDINARY TRAUMA

Case Age	History	Diagnosis	Interval till surgery	Hospital treatment*	Result
1 4	Riding scooter in stable yard, fell injuring right leg	Compound fracture right tibia simple fracture fibula	6 hrs	Steinmann pin, skeletal traction	Primary healing
2 10	Jeep collided with civilian car	Compound fracture right elbow olecranon and humeral articular surface	7 hrs.	500 c.c. plasma. Insertion of steel wire	Primary healing
3 3	Jeep collided with civilian car	(1) Compound fracture right tibia and fibula (2) fracture left femur (3) multiple lacerations of scalp	1½ hrs.	Insertion of T & G bone plate	Minor serous discharge
4 31	Caught right hand in circular buzzsaw	Lacerated wound, splitting middle right finger longitudinally extending dorsum of hand to wrist. Laceration of flexor and extensor tendons	1 hr	Amputation of finger	Primary healing
5 27	Right index finger cut off with power saw	Compound fracture of middle phalanx, right index finger	1½ hrs.		Minor serous discharge
6 36	Caught right thumb in lock of searchlight	Compound fracture of distal phalanx, right thumb	2 hrs		Healed for primary
7 22	Index finger caught on muzzle of gun	Compound fracture of distal phalanx right index finger	5 hrs.		Primary healing
8 25	Thrown from truck striking wrist and forearm on pavement	Compound fracture right radius and ulna. Simple fracture right navicular	5 hrs	Later reduction fracture of ulna	Primary healing
9 19	Motorcycle collided with truck	Compound fracture left tibia, Colles fracture left. Simple fracture scaphoid, left	6½ hrs.		Primary healing
10 23	Jumped to catch football landed on extended right great toe	Compound dislocation right great toe	5 hrs		Primary healing
11 34	Jeep overturned striking left forearm	Compound fracture left radius	12 hrs.		Primary healing
12 21	Struck by auto while crossing street	Compound fracture right tibia, simple fracture right fibula. Laceration of forehead	3 hrs.		Primary healing of wound. Phlegm on left leg
13 10	Driving car dazed hit tree	Compound fracture left tibia involving knee joint	2 hrs	Plaster cast	Primary healing
14	Struck left hand against piece of glass on street	Compound fracture proximal phalanx, 4th finger left laceration extensor tendons left index, middle and ring fingers	6 hrs.	Plaster cast	Primary healing
15 3	Stumbled, falling striking finger against gun during drill	Compound fracture middle phalanx left forefinger	3 hrs	Pin pulp traction	Primary healing
16 23	Jeep overturned driving blackout injuring right hand	Severe lacerations dorsal surfaces, 3d, 4th and 5th fingers exposing middle and distal phalanges and interphalangeal joints	1 hr	Closure of as much of wound as possible	Healed without infection
17 4	Struck by auto with extensive laceration right hand and buttock	Laceration of extensor tendons of 2nd and 3d fingers, brush burn of back of hand	5 hrs.	Tendon repair primary closure	Healed for primary
18 3	Caught 4th finger in 155 mm breech block	Compound fracture of distal phalanx left 4th finger	1½ hrs		Healed for primary

\*General treatment as outlined in text.

in detail as an example of fractures ordinarily seen in civilian practice

The patient, a 19 year old male, was thrown to the pavement from a jeep at 7 00 a.m. on June 9, 1942, as a result of a head-on automobile collision. He was rendered unconscious for 2 hours and was admitted to the hospital in shock. There were multiple abrasions about the forehead, shock and a compound fracture of the right olecranon involving

the elbow joint. The laceration over the site of fracture was about 3 inches long, and this wound communicated with the joint. The fracture was of a transverse comminuted type with a separation of about one half inch between the fragments. In addition there was a V-shaped vertical fracture through the distal midportion of the trochlea and external condyle of the humerus. There was considerable debris in the wound. The red blood cell count was 4,100,000, white cell count 9,950, and the urine ex-

TABLE II—COMPOUND FRACTURES FROM GUNSHOT WOUNDS

Cases Age	History	Diagnosis	Interval to surgery	Flap(s) treatment(s)	Result
36 37	Gunshot wound, hand	Compound fracture			Primary union
38 38	Gunshot wound, left hand	Compound comminuted fracture, proximal phalanx, left forefinger Below incised wound of hand	5 hrs.	Flap pulp traction	Healed by granulation tissue growth
39 36	Gunshot wound, left knee	Wound, left knee joint Compound fracture left femur	24 hrs.	excised caria made sulfonamide solu- tion upon knee joint Partial wound closure	No infection. Scar in wound healed by granu- lation
40 35	Gunshot wound, middle finger left	Compound fracture, middle left finger at phalanx	hrs.		Primary union
41 30	Gunshot wound, left index finger middle phalanx	Compound fracture middle phalanx, left index finger	2 1/2 hrs.		Primary healing
42 34	Gunshot wound, right great toe	Compound fracture, right first meta- tarsal and phalanx	8 hrs.	Treated with some sulfonamide powder and vas- eline pack. Flap over end	Primary union except in between great and sec- ond
43 31	Gunshot wound, left lower leg	Compound fracture lower left tibia	hrs.		Primary healing
44 36	Gunshot wound, entering right ankle medially going through joint, wound at exit below lateral malleolus	Compound fracture, tibia cuboid, an- chilus, right		Treated at another hospi- tal, debridement, vascular stump, phalanx, pedicle, made easily. Debridement thorough, pus, drains, dressed with carbolized, then sulfonamide and cast	Wound healed by granu- lation. Good result
45 37	Gunshot wound, entry above right patella through quadriceps pouch and left tibia	Fracturing wound right knee joint. Compound fracture left tibia	2 1/2 hrs.		Both wounds healed by primary
46 35	Gunshot wound, pistol, left elbow	Compound fracture left humerus. Dis- section of brachial artery Compound wound left elbow		Treated at postling hospi- tal, debridement, vascular stump, pedicle, pedicle, made easily. Debridement thorough, pus, drains, dressed with carbolized, then sulfonamide and cast	Open infection. Cellulitis osteomyelitis
47 30	Gunshot wound, right foot	Compound fracture right third meta- tarsal	none	Application of cast	Primary heal
48 30	Gunshot wound, palm	Compound fracture left third meta- carpal	hrs.	Cast with pulp traction	Primary healing

\*General treatment as outlined in text

amination, normal. On drainage 500 cubic centimeters of blood plasma was administered intravenously. The wounds were sprinkled with carbamide sulfonamide mixture powder dry dressing and Ace bandage were applied and the fracture was splinted. At 100 p.m. after patient regained consciousness and recovered from shock, formal surgery was done.

Under gas-oxygen-ether anesthesia the wound and elbow were scrubbed with soap and water for 30 minutes followed by irrigation with 500 cubic centimeters of normal saline and then 500 cubic centimeters of saturated carbamide sulfonamide mixture solution. The skin edges were excised for distance of one-quarter of an inch and all devitalized fat, muscle and fascia as removed. Irrigation of the wound was repeated. Two drill holes were then

made in the distal fragment and one in the proximal fragment. A piece of stainless steel wire was passed through one hole and around the proximal fragment under the triceps tendon. A second piece of wire was placed through the other drill hole in the distal fragment and through a hole in the proximal fragment. The fracture was reduced by traction and twisting the wires drawing the fragments in apposition (Fig. 1). A small loose bone fragment of the external condyle of the humerus was fixed. Carbamide sulfonamide mixture powder was sprinkled into the elbow joint and throughout the cast. The skin was approximated with interrupted 1/2 mattress sutures. Dry dressing and an Ace bandage were applied. The arm was immobilized in a splint with the elbow flexed to a right angle.

Ten thousand units of gas gangrene antitoxin and a 1 cubic centimeter "booster" dose of tetanus toxoid were injected after operation. One gram of sulfathiazole was given orally four times a day for the next 8 days. Temperature prior to operation was 101 degrees, pulse, 90, and respiration, 20. On the first postoperative day, temperature reached 101.8 degrees, 100 degrees on the second, and 99 degrees on the third, thereafter remaining normal until the 21st postoperative day when there was an elevation of 101 degrees because of a slight upper respiratory infection which subsided after 3 days. When the wound was inspected on the 9th postoperative day it showed healing *per primam*, the splint was removed, and active motion was started. Half of the sutures were removed on the 12th postoperative day and the remainder on the 15th postoperative day. The blood sulfa level on the 6th postoperative day after 15 grams sulfathiazole was 4.3. The red and white blood cell counts and urine examinations were normal throughout the postoperative course. Physical therapy was started on the 16th postoperative day. This consisted of infra-red heat and active exercises, and later the carrying of a 5 pound weight. The patient was discharged from the hospital on the 34th postoperative day with active flexion to 65 degrees, extension of 162 degrees, and normal supination and pronation. There were no complaints of pain in the elbow. The wound healed by primary intention.

#### COMPOUND FRACTURES RESULTING FROM GUNSHOT WOUNDS

Twelve gunshot wounds are tabulated in Table II. All of these resulted in compound fractures and were incurred principally at close range. The time interval between the accident and operation varied from 15 minutes to 16 hours. Two patients were treated elsewhere and received by transfer several days after injury. Both of these patients had been treated by débridement, sprinkling the wound with sulfanilamide powder, gauze packing, plaster immobilization, and leaving the wound open. One patient had developed a chronic osteomyelitis which eventually healed by packing with carbamide sulfonamide mixture powder and plaster immobilization. In the other patient, the brachial artery had been severed in the antecubital fossa and gross infection had developed. There was inadequate circulation in the arm which may explain the inability of the subsequent combined chemotherapy treatment to control the infection. A guillotine amputation of the arm, proximal to the wound, was done on the 16th day after injury. The wound was treated by means of

carbamide sulfonamide mixture and adhesive skin traction and healed rapidly. Eight of the 10 wounds under initial treatment at this hospital healed *per primam*. In 2, the tremendous damage, extensive laceration, and loss of skin and blood supply excluded any hope of primary union—our hope being to save the great toe (Case 24) and the finger (Case 20). Both of these wounds healed by granulation and the digits were preserved. There were 2 instances in which the knee joint was involved, both healed without infection and with good joint motion. In 1 patient, 55 cubic centimeters of saturated carbamide sulfonamide mixture in distilled water was injected into the knee joint after closure of the wound. The following case report will serve as an example of our treatment of gunshot wounds.

A 23 year old soldier, Case 30, was admitted on July 1, 1942, with a gunshot wound of the left hand. A dry dressing and tourniquet were applied at the first aid station. The general physical examination on admission was essentially normal.

There was a stellate wound of entry in the palm of the left hand about 5 centimeters across with a V-shaped wound of exit on the dorsum about 6 centimeters by 8 centimeters. There was much destruction of tissue, a comminuted fracture of the shaft of the third metacarpal bone, and the flexor tendons of the index finger were widely exposed and burned with powder.

Under local novocain block, extensive débridement of the wounds was accomplished. The skin and wounds were washed with soap and water, irrigated with saline, and saturated carbamide sulfonamide mixture solution. The skin edges and devitalized tissue were excised. Two loose fragments of the third metacarpal bone were removed. The tendons were intact but the flexor to the index finger was severely burned. Bleeding vessels were tied with No. 0 catgut. Carbamide sulfonamide mixture powder was liberally sprinkled throughout the wounds. The skin was closed loosely with interrupted silk sutures and a pin was placed through the pulp tip of the third finger for traction. The hand was immobilized in a circular plaster cast from below the elbow to the metacarpophalangeal joints.

The postoperative care included sulfathiazole orally, 1 gram four times a day, a stimulating dose of tetanus toxoid, (1 cubic centimeter) and 10,000 units of gas gangrene antitoxin.

Convalescence was uneventful—temperature reaching 99.8 degrees on the 2d and 5th postoperative days. On admission, the red blood cell count was 4,980,000, white blood cell count, 14,300, polymorphonuclear leucocytes, 77 per cent, and



TABLE III—SHELL FRAGMENT INJURIES

Case No.	History	Diagnosis	Emergency Treatment	Interval till surgery	Hospital treatment*	Result
21	Shell fragments struck in neck and right shoulder	(1) Compound fracture right humerus (2) Penetrating wound of neck	Wounds sprinkled with carbamide sulfonamide mixture dry dressing, fracture splint, eye patches	2 1/2 hrs.	Insertion T & G bone plate, tracheotomy	Healed by primary
22	Shell fragments in right shoulder and left knee	(1) Compound fracture right clavicle (2) Abrasion left knee	Wound sprinkled with carbamide sulfonamide mixture	3 1/2 hrs.	Removal of shell fragment, dress changed	Healed by primary
23	Shell fragments in both elbows	(1) Extensor pharynx (2) compound fracture left radius, humerus, ulna, (3) compound fracture right radius	gas c. pharynx 300-c.c. tracheotomy, wounds sprinkled with carbamide sulfonamide mixture, fracture splinted	hrs.	gas c. pharynx 300-c.c. tracheotomy, ray therapy 5 treatments	Left hand in primary, right in primary
24	Shell fragments left hand and both shoulders struck	(1) Compound fracture of left ul and 2d metacarpals, (2) Compound fracture left 2d, 3d, and 4th metacarpals, (3) Laceration, extensive of left hand, (4) Laceration right and left shoulders	Wounds sprinkled with carbamide sulfonamide mixture powder and dry dressing applied	6 1/2 hrs.	Setters of fractures	Primary healing
25	Shell fragments in left chest, shoulder and right hand	(1) Compound fracture 2, 3, 4, 5 metacarpals, right (2) Laceration extensive hand, 2d (3) Multiple lacerations right hand, face and left shoulder	Wounds sprinkled with carbamide sulfonamide mixture powder and dry dressing applied	7 1/2 hrs.	Trachea extubated, dress changed	Primary healing
26	Shell fragments	Wound penetrating right knee joint	Wound sprinkled with carbamide sulfonamide mixture	1 1/2 hrs.	Removal of shell fragment	Primary healing
27	Shell fragments both thighs	(1) Extensive wounds both thighs, (2) Laceration left femoral artery	Wounds sprinkled with carbamide sulfonamide mixture, dry dressing, compression bandages, left leg splinted	hrs.	Wounds sprinkled with carbamide sulfonamide mixture, wound left open	Gas gangrene, amputation
28	Shell fragments right side of head	Wound, lacerated right parietal region head	Sprinkled with carbamide sulfonamide mixture	6 1/2 hrs.		Primary healing
29	Shell fragments left and right thighs	Wound, lacerated extensive left thigh and right thigh	Sprinkled with carbamide sulfonamide mixture	8 1/2 hrs.	Dress changed and closed	Healed by primary
30	Shell fragments face	Wounds, fracture of face	Sprinkled with carbamide sulfonamide mixture	hrs.		Primary healing
31	Shell fragments abdomen	Wound, lacerated, of abdomen	Sprinkled with carbamide sulfonamide mixture			Primary healing

\*Usual treatment as outlined in text.

lymphocytes, 3 per cent. The urine was normal, Kahn negative. The blood sugar determination on the 3d postoperative day was 5 milligrams per cent red blood cell count, 300,000 white blood cell count, 800. Sulfathiazole as discussed on the 8th postoperative day. Traction and sutures were removed on the 3d postoperative day. The wound had healed *per primam*. Physiotherapy consisting of hip pool and active finger exercises was started.

It is recognized that novocain infiltration anesthesia in contaminated wounds is not desirable as well as being a sulfa drug inhibitor. Block anesthesia represents no contraindication so far as we can determine.

#### SHELL FRAGMENT INJURIES

Our experience with carbamide sulfonamide mixture was limited to the ordinary compound fracture and gunshot wounds until a Howitzer gun explosion occurred which resulted in several typical wartime casualties (Table III). The more important injuries consisted of 3 patients with lacerations of tendons of the hand and compound fractures of the femoral artery and extensive thigh wounds, 4 soft tissue wounds, 1 penetrating wound of the knee joint and 3 intra-abdominal injuries. One patient with extensive

abdominal injuries died within 12 hours from a secondary renal hemorrhage. All the others survived. These cases illustrate the treatment of compound fractures, tendon injuries, joint, arterial and abdominal wounds, gas gangrene, the value of blood sulfa determinations, and the necessity for frequent blood counts, plasma and blood transfusions. This accident served as an introduction to actual war surgery and the efficiency of carbamide sulfonamide mixture in the treatment of war wounds.

The urgent necessity of having large amounts of plasma ready for immediate use was amply demonstrated. Several patients arrived in extreme shock and the immediate use of plasma undoubtedly saved their lives. For example the blood pressure of one patient could not be recorded on arrival at the hospital, his pulse was not palpable and the heart sounds barely audible. Fifteen hundred cubic centimeters of plasma, 500 cubic centimeters of citrated blood and oxygen were necessary to combat his immediate shock. It is our impression that plasma should be available for use in the first aid station prior to, or during, transfer of patients to a hospital. Although these patients arrived at the hospital 1 to 1½ hours after the accident, operation in the seriously injured, other than the intra-abdominal cases, was delayed many hours



Fig 1 Case 2 Compound fracture of olecranon and humerus treated with carbamide sulfonamide mixture. Wound healed by primary union.

until shock had been successfully overcome. Plasma and blood transfusions were used freely. As the patients were received, carbamide sulfonamide mixture was sprinkled over the wounds, and dry dressing, Ace bandage, and splints were applied. The patients were then operated on in the order of the severity of their injury. All received tetanus toxoid in 1 cubic centimeter stimulating doses, oral sulfanilamide or sulfathiazole after operation, with frequent red, white, and differential counts and blood "sulfa" determinations. A typical case history follows.

A 22 year old sergeant, Case 31, was looking up in the air when he was struck in the neck and right



Fig 2 Case 30 Compound fracture, third metacarpal from .30 caliber gun treated with carbamide sulfonamide mixture. The wound healed by primary union.



Fig 3 Case 30 Roentgenogram which was made after the compound fracture of the third metacarpal had been reduced.

boulder by shell fragments. On being hit he spun around and knocked over. Large amounts of bright red blood were expectorated. There was no pain at all for about 45 minutes.

Upon arrival at the hospital the patient was coughing and raising bright red blood. He was unable to talk above a whisper. There was laceration on both sides of the neck just above the thyroid cartilage and each wound was about three finger breadths from the midline. The right side of the neck was tender and swollen, there was no crepitus present. Blood was exuding from the nose. On the anterolateral aspect of the right shoulder there was a large ragged wound measuring 6 by 4 inches involving underlying fascia, deltoid muscle, and extending down into the humerus which presented badly comminuted fracture (Fig. 4). There were wounds of entry on the dorsum of the shoulder joint and superior wall of the axilla as well as lacerations in the axilla and posterior aspect of the shoulder. His blood pressure was 118/60 pulse 88. The remainder of the physical examination was within normal limits.

First aid treatment consisted of sprinkling carbamide-sulfonamide mixture powder on the neck and shoulder wounds, and the application of dry dressing and bandage. The right arm was immobilized.

Thomas arm traction applied. Two hundred and fifty cubic centimeters of plasma was given intravenously and cubic centimeter of tetanus toxoid subcutaneously. Eight hours after injury definitive surgery was carried out. Under intravenous pentothal all wounds except those of the neck were cleaned with soap and water and irrigated with normal saline. Skin edges and injured tissue were excised and irrigation of the wounds was repeated. The fracture of the humerus was reduced and immobilized with Townsend and Gillman bone plate (Fig. 5). Carbamide-sulfonamide mixture powder was dusted into the wound and the skin was closed loosely with interrupted silk sutures. Without drainage. A fragment of shell in the wound was searched for but not found. The arm was immobilized in posterior molded plaster splint.

Postoperative care included sulfanilamide orally gram 6 times a day and intravenous glucose and saline to maintain the fluid intake. The temperature on the second postoperative day reached degrees, fluctuated between 98.6 and degrees until the third postoperative day thereafter remaining normal. Red blood cell count on the 4th postoperative day was 750,000 white cell count 7,850 alpha determination 4. On the 4th postoperative day the patient received transfusion of 500 cubic centimeters of citrated blood. On the 6th postoperative day the red blood cell count was 390,000 white cell count 8,500 and blood sulfas 3.5. A second transfusion of 500 cubic centimeters of blood was given. The patient was expectorating considerable mucus and had some difficulty in swallowing and talking. The wound on the left side of the neck was healed. That on the right as draining slightly.

The shoulder wound was dressed on the 4th postoperative day and wound healing was progressing. On the 6th postoperative day red blood cell count was 3,200,000 white cell count was 2,250 hemoglobin 0.5 grams differential polymorphonuclear leukocytes 69 per cent lymphocytes 21 per cent sulfas determination 5.6 milligrams. Oral sulfanilamide was discontinued on the 7th postoperative day. Sutures were removed on the 8th day and the wound healed without infection. Due to tenderness in the skin at the upper portion of the wound there was slight separation of the skin edges. The plaster splint was removed and the patient underwent physical therapy department for heat, massage, and abduction exercises. The remainder of his convalescence was uneventful. Motions of the shoulder abduction, flexion, extension, and rotation were normal, and elbow motions were normal. Because the upper portion of the anterior wound was adherent to underlying tissue, this was later excised and resutured. The fracture of the humerus healed by bony callus.

#### EVALUATION

Carbamide-sulfonamide mixture when sprinkled over a fresh wound tends to inhibit the growth of bacteria and chemically debrides devitalized tissue. In this way when large numbers of casualties are brought in at the same time emergency treatment may be given and patients operated upon in the order of the urgency. In case definitive surgery must be delayed because the patient is in shock or has to be transferred from battalion aid station to larger installations the emergency use of carbamide-sulfonamide mixture would appear to be most important. When the wound is sprinkled with this powder and dry dressings are applied, surgical operation may be delayed and primary closure even attempted long after 6 hours have elapsed.

The danger of using chemicals in traumatic wounds is that the surgeon may err in placing too much reliance on the drug. Baker in reporting the use of sulfonamides in traumatic and infected wounds, warns that with the use of drugs one is apt to acquire a false sense of security and become lax in following established surgical principles. There is no substitute for thorough and skillful surgery. The surgeon must achieve the gross debridement. Carbamide-sulfonamide powder does not remove necrotic tissue and produces macroscopic debridement. It tends to rid the wound of sulfanilamide inhibitors, such as penicillin.



Fig 4 Case 31 Compound fracture of right humerus from shell fragment of 60 millimeter Howitzer, treated with carbamide sulfonamide mixture Wound healed *per primam*



Fig 5 Case 31 Roentgenogram made after the compound fracture of the right humerus had been reduced and a Townsend Gilfillan bone plate had been inserted

débris, and split protein products. The efficiency of sulfanilamide depends on the amount of sulfa inhibitors and also on the amount of sulfanilamide in solution. The carbamide increases the solubility of sulfanilamide and renders the drug about ten times more effective. The carbamide sulfonamide powder causes no burning or sensation of pain when applied to the wound.

The primary closure of contaminated traumatic wounds, particularly those involving fractures, is a question about which there is considerable difference of opinion. Whether or not it is attempted must depend upon the nature of the wound, facilities and circumstances, as well as the skill of the surgeon. The experience of war surgeons dictates that actual war wounds should never be closed by primary suture but packed open loosely. Key (9) referring particularly to compound fractures states that it has been his custom to close such wounds by primary suture after a careful débridement and expect primary healing. By the use of sulfanilamide or sulfathiazole in the wound, or a mixture of the two, he points out that a wound can be

sutured with more assurance than formerly and points to the experience of himself (10) and others (7, 8). We believe that the carbamide sulfonamide preparation is an improvement over any of the sulfonamides used in mixtures or alone. It is obvious that in the formal treatment of traumatic wounds primary closure after satisfactory wound hygiene is advisable whenever possible. To allow a preparation such as carbamide sulfonamide to function, it must be kept in the wound. Leaving the wound open allows the mixture to drain out and therefore diminishes its effectiveness. The 2 cases of gross wound sepsis which received initial treatment with the carbamide sulfonamide mixture method we feel were due to failure to achieve effective debridement of the wound.

In Case 37 effective débridement was not possible since the thigh wound was extensive and the muscle so severely contused that removal of all injured tissue was impossible. This wound was covered with carbamide sulfonamide mixture, vaseline gauze, dry dressing, and Ace bandage. The skin was not closed. The femoral artery had been completely severed. Swelling of the leg occurred with subsequent development of gas gangrene. This was our only case

of this type of infection and occurred in a wound in which primary closure was not attempted. The patient received sulfanilamide orally and parenterally. His blood sulfa level was 2 milligrams per cent when gas infection developed. A successful result was accomplished by gillotine amputation.

Ray therapy sulfanilamide orally, daily local application of carbamide sulfonamide and 0.0000 nitro of gas gangrene antitoxin intramuscularly. It is not possible to determine which was the most effective of these remedies but it is our impression that amputation, ray therapy and local application of the carbamide sulfonamide mixture were the most important. In Case 33 patient had both elbow struck by shell fragments resulting in compound fractures of humerus, olecranon, radius, and destruction of the elbow joint on the left and compound fracture of the radius on the right. The injuries were so serious that one consultant thought amputation necessary. Both wounds were treated by the routine described here. The left, which was the more extensive wound, healed *per primam*; the right developed a gross infection, sutures were removed and the wound thoroughly opened. Using frequent carbamide sulfonamide mixture dressings, irrigation with saturated carbamide sulfonamide mixture solution, the wound healed. It is believed that failure to attain satisfactory healing of the right wound was due to unsatisfactory débridement.

The one other case requiring amputation was in a gunshot wound of the elbow with severance of the brachial artery previously related. In the last war it was said that when the main vessel of a limb is cut and the wound extensive amputation is almost inevitable. These 2 cases, 1 of the femoral artery and the other the brachial, indicate the truth of this observation.

Cleansing the wound by irrigation with carbamide sulfonamide mixture solution is important and should be thorough. An antiseptic may be applied to the skin but never to the wound. A solution strong enough to kill bacteria will injure tissue cells, thus retarding their natural resistance. Irrigation with large amounts of solution produces a mechanical cleansing and should always be used as an adjunct to surrounding skin preparation. Scrubbing and irrigating require time and are apt to be omitted or performed hastily. Nevertheless they constitute important steps in proper wound hygiene. In several wounds, tissue drains were inserted. This is a compromise between the open and primary closure treatment. Drains, of course, allow

the carbamide sulfonamide mixture chance to escape and so lessen or diminish their local action. Furthermore the introduction of it permits the formation of a fluid level, thus preventing contact of the mixture to the whole wound. Drains may also introduce infection; they cause a foreign body reaction and encourage scarring. When immobilization of a fracture is achieved by plaster of Paris, the cast, unless there is elevation of temperature, pain or swelling, should not be disturbed for several weeks. Windows in the cast are not recommended.

Although this group of patients is small it may be worth while noting that the incidence of severe infection in 32 compound fractures from injury gunshot or shell fragments receiving original formal surgery at this hospital is 3.1 per cent and all infections include those with serous drainage is 15.6 per cent. This compares favorably with those reported by Baker of 10 per cent severe infection, 21.9 per cent for all infections and Campbell and Smith of 18.1 per cent for all infections.

Primary closure of wounds may be done safely when they are under close observation and when facilities are available for continued observation of the patients. Primary suture should never be done if thorough débridement and effective wound hygiene cannot be accomplished because of the extent of the injury or lack of time. Under those circumstances, the method advocated by Trott or Orr is recommended. If infection develops after closure the skin sutures may be removed and the wound treated as an open one without fear of any added complications.

Unless there are definite indications, the dressings should not be disturbed until the 10th postoperative day. Frequent inspection of the wound is apt to lead to complications. It is said that "wound curiosity has cost many graves." Half the skin sutures can be removed on the 10th postoperative day and the other half on the 12th. It is our impression that carbamide sulfonamide mixture is as effective as sulfanilamide, slightly delays wound healing and retards epithelialization. It accelerates granulation tissue formation. At the stage of epithelialization necessary for the use of carbamide sulfonamide mixture has passed.



Fig 1 Case 1 a, Anteroposterior view both ankle joints, the left ankle is normal, b, lateral view of right ankle joint,

c, lateral view of right ankle, 2 months after fusion, d, lateral view, right ankle, 8 years after operation

unilateral limp were present in varying degree in the different patients. There were five patients who had, before operation, draining sinuses, and 3 patients with healed sinus scars. The duration of symptoms previous to operation varied from 6 weeks to 26 years, the average duration being 5 years. Twelve of the 25 cases had a duration of less than a year. In the 13 remaining patients the durations varied between 1 and 5 years in the majority of cases.

#### DIAGNOSIS

A presumptive diagnosis of tuberculosis of the ankle joint was made before operation on clinical, x-ray, and laboratory findings. The x-ray findings are of considerable help in establishing the diagnosis, the important feature being a general decalcification of the bone with an associated well defined joint effusion. The presence of bone atrophy, thinning of the joint space, erosion of the articular cortex, and, in the more advanced cases, actual destruction of the bone are also helpful. These findings are not pathognomonic, but when present should make one strongly suspicious of a tuberculous infection. The presence of an elevated sedimentation rate points to an inflammatory process. The absence of a positive Mantoux test is of value in ruling out tuberculosis, since it is most unusual to have a tuberculous joint in the presence of a negative test.

A positive diagnosis of tuberculosis was established in all cases either by frozen section or by the usual pathological section of material

removed at the time of operation. It is felt that this is of great importance in evaluating end-results in any group of tuberculous joints.

#### PREVIOUS TREATMENT

Various types of treatment had been tried on this group of patients before arthrodesis was performed. Most of this treatment was carried out elsewhere, since at this hospital immediate arthrodesis of a tuberculous joint is recommended unless the general condition contraindicates it. The most common forms of treatment were incision and drainage of abscesses, leg casts, and braces. Incision and drainage was done in 8 cases, in some of the cases this was done two or three times. It is doubtful if this form of treatment is ever indicated in a primary tuberculous infection. It usually leads to fistula formation and the development of secondary infection. In some instances when secondary infection is already established, incision and drainage may be necessary as a temporary measure.

Eight patients wore casts or posterior splints for varying periods of 2 months to 1 year. Ankle braces were worn by 6 patients from 3 months to 2 year periods. Two patients were kept in bed for approximately a year's time. Four patients were treated with adhesive strapping, 1 had the ankle manipulated and another had baking and massage. Four patients had no treatment previous to the arthrodesis. This summary of treatment is not intended to give the impression that conservative treatment in these cases was given an



Fig. 1. Case 1. a, Anteroposterior view of both ankle joints, the left is normal. b, Lateral view of right ankle joint. c, Lateral view right ankle 14 years after operation. d, Lateral view right ankle, 13 years after operation.

adequate trial conservative treatment had been tried in another large group of cases and the results reported before arthrodesis was accepted as the best form of treatment.

#### TECHNIQUE OF ANKLE FUSION

The type of arthrodesis performed in this group of cases is a fairly simple procedure. The ankle joint is exposed through an anterior incision, with care to avoid the dorsalis pedis artery and the extensor tendons. The articular cartilage of the tibia and the talus, including that of the malleoli is removed as completely as possible together with exuberant tuberculous granulation tissue. If any bone cavities are found, they are thoroughly curet-

ted. One must be careful not to damage the distal epiphyseal plate in patients of the younger age group. Following the removal of the articular cartilage, it should be possible to secure apposition of raw bleeding bone surfaces. Bone chips are then removed from the tibial shaft and are jacked into any spaces remaining in the joint and across the anterior aspect of the joint. The wound is closed in layers and a long leg cast is applied with the foot held in the optimum position of dorsiflexion usually 100 to 110 degrees.

#### PATHOLOGY

This type of operation affords excellent opportunity for the study of the gross characteristics of tuberculous joint infections. The findings varied with the particular case and the description varied with the surgeon. The joint capsule frequently bulged anteriorly and was thickened and edematous. The synovial membrane was replaced by abundant grayish yellow avascular friable granulation tissue. The articular cartilage frequently was thin, lacked luster and separated easily from the underlying bone and in some places was completely absent. Cavities in the adjacent bone of the talus or tibia were frequently present and filled with bone debris, caseation or granulation tissue. Cavities were fairly frequent in the head and neck of the talus. In some cases the disease process had extended into adjacent tendon sheaths or had invaded the fossa beneath the talar head and thus by direct extension into the talocalcaneal joint.



Fig. 3. Case 3. a, Left, Lateral view right ankle joint. b, Anterior view right ankle 1 year after operation.





necessarily mean hospital care since most patients, if the progress is satisfactory, can be discharged from the hospital in 3 to 6 months and the cast changed in the clinic as necessary.

#### ROENTGENOGRAPHIC FEATURES OF TUBERCULOSIS OF THE ANKLE

Some of the characteristic x ray findings in tuberculosis of the ankle are shown in the accompanying roentgenograms. The x ray appearance during certain stages of treatment and the final end-result are also shown.

**CASE 1.** Patient as a girl of 3 years, had had the disease years. Previous treatment had been given except trapping of the ankle. The anteroposterior view (Fig. 1) of the right ankle shows definite effusion, bone atrophy and thinning of the joint space. There is no bone destruction. The opposite normal ankle is shown for comparison. Figure 2 is a lateral view of the right ankle. The joint effusion is more definite and easily visualized. Figure 3 was taken 6 months after fusion. There is less evidence of active infection. The fusion is not yet solid and discreet bone chips are still present. Figure 4, taken 8 years after operation, when patient was 11 years of age, shows the ankle joint solidly fused. The bone appears healthy; there is no evidence of activity. The epiphyseal line is intact showing that successful fusion can be obtained without interfering with growth. Clinically the patient has an excellent result.

**CASE 2.** The patient was 3 years of age and the disease, present for 6 months, had been treated with an ankle brace for 3 months. Anteroposterior view (Fig. 2a) of the right ankle shows the characteristic ray appearance of tuberculosis. The opposite ankle is normal. Figure 2b is a lateral view of the right ankle showing the marked joint effusion. Figure 3c, lateral view of right ankle 3½ years after operation, shows that fusion is solid. The bone is healthy and the epiphyseal line is intact. Figure 3d, a lateral view of the right ankle, 3 years after operation when patient was 6 years of age, shows the final end-result with solid fusion and healthy bone. The epiphyseal line has closed.

**CASE 3.** The patient, 4 years of age, had had the condition 6 months. Previous treatment consisted of incision and drainage shortly after onset. Clinically the patient presented such severe picture with marked swelling and draining sinuses that amputation was considered. Figure 3a before operation shows the marked effusion with destruction of the superior portion of the talus. Figure 3b lateral view was taken 2 years after fusion. Because of involvement of the talocalcaneal joint, this joint was also fused. Both the ankle and talocalcaneal joints are solidly fused. There is no effusion or soft tissue reaction although the bone does not yet appear as healthy and contrastable as in previous cases. There is no evidence of activity.

#### END-RESULTS

In the end result study of these 25 patients, the follow up period varied from 1½ years to 13½ years, the average follow up period being 6.2 years. An end result was classified as excellent if it met the following criteria: a solid fusion in good position of 100 to 105 degrees dorsiflexion; no draining sinuses, no swelling or tenderness; no pain either at rest or on weight bearing; normal gait, normal activities, and final roentgenogram showing bony fusion with healthy appearing bone. A result was classified as good if it met all but one or two of the requirements for an excellent result. A result was classified as fair if the fusion was considered doubtful on x ray examination and a brace considered advisable although symptoms were slight.

On the basis of outline given 16 or 64 per cent of the cases had an excellent result, 6, or 24 per cent, of the cases had a good result, and 3, or 12 per cent of the cases had a fair result. Combining the excellent and the good results makes a total of 88 per cent satisfactory results. I consider the fair results in this group as being a better end result than amputation.

In the 9 cases with talocalcaneal joint involvement, the results were excellent in 4, or 44 per cent, good in 4, or 44 per cent and fair in 1 case. Again the percentage of satisfactory results is 88 per cent.

#### ANALYSIS OF STUDY

These cases were not selected for operation. Every patient with strongly suspected tuberculosis of the ankle joint, with the exception of those having an active lung lesion, was advised to enter the hospital for further observation and treatment. At operation an arthrodesis was done if the frozen section was positive for tuberculosis or if the gross appearance was that of tuberculosis. In the cases in which a frozen section was not done the routine tissue sections were positive for tuberculosis in all cases.

Some patients in poor general condition were given a preliminary rest period of 4 to 6 months at the Country Branch of the Hospital. One 3½ year old patient came in with a markedly swollen ankle and 6 profusely draining sinuses. The attending surgeon made the



## SOME MANIFESTATIONS OF REGIONAL ILEITIS OBSERVED SIGMOIDOSCOPICALLY

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**R**ELATIVELY little attention has been given in the literature to the anorectal findings in cases of regional ileitis. Ever since 1933 when Crohn and his co-workers established regional ileitis as an entity, we have been impressed with the frequency of certain anorectal manifestations of the disease. We reviewed the records of 114 consecutive cases of regional ileitis in which the diagnosis was made by roentgenologic examination and confirmed by exploration and in which sigmoidoscopic examinations were made. The purpose of the review was to note the lesions of the lower part of the bowel which are more or less peculiar to the disease. We found the following conditions to be characteristic: (1) anal abscess and anal fistula, (2) extrarectal mass, (3) anal ulceration and anal contraction. One other condition, ulceration of the lower part of the bowel, was found in a few cases after short circuiting operations.

### ANAL ABSCESS AND ANAL FISTULA

Much attention has been called to the tendency to fistulization in regional ileitis, that is, fistulas tend to originate in the involved ileum and terminate in the abdominal wall or an adjacent viscus. In 1938, Penner and Crohn pointed out that this tendency to fistulization also gave rise to anal fistula and that, in many instances, the first clinical manifestation of the disease might be anal abscess or anal fistula. This manifestation might even precede consciousness on the part of the patient that intestinal function was disturbed. Eight, or 14 per cent, of Penner and Crohn's 50 patients had anal fistula.

Thirty-six, 31.6 per cent, of our 114 patients had anal abscess or anal fistula, or they gave a history of having had an operation for anal fistula within a period of 3 years prior to their visit to the Mayo Clinic. This is more than twice the incidence reported by Penner and Crohn, but they pointed out, and we agree, that unless the patient is carefully questioned past or present existence of the condition may easily be overlooked.

Eight, 7 per cent, of the 114 patients with regional ileitis came to the clinic primarily because

of anal fistula. The regional ileitis as so mild that the patient was not conscious of any intestinal disturbance. In 6 of these 8 cases anal fistulectomy was performed without a awareness of the regional ileitis being aroused. The regional ileitis was discovered subsequently within a year or two, when symptoms of the intestinal disturbance appeared. Study of these cases and also of the cases in which operation was performed elsewhere indicates that with increased alertness to the possibility of coexistence of the two conditions, even more cases of regional ileitis could be found among patients whose primary complaint is anal abscess or anal fistula.

### EXTRARECTAL MASS

A mass was palpable in the rectocolic or rectouterine space in 20, or 17.5 per cent, of the 114 cases. This mass, of course represents an involved segment of diseased ileum perhaps complicated by pelvic peritonitis and dense fibrous tracts. An extrarectal or pelvic mass is generally recognized as being a frequent finding in cases of regional ileitis. Its presence is mentioned here only for emphasis. Recently we studied the nature of extrarectal masses, produced by lesions of the colon or small intestine in 58 cases. We found that in 29 cases the extrarectal mass was due to carcinoma of the colon. In 26 cases it was due to diverticulitis. In only 3 cases was it due to regional ileitis. Therefore if all conditions which will produce extrarectal masses are taken into consideration regional ileitis accounts for only a small percentage.

### ANAL ULCERATION AND ANAL CONTRACTION

Considering the nature of the infected fecal content which is transported to the anal region and the vulnerability of the anal crypts to infection, inflammatory reactions aside from abscess and fistula should be common. Nine, 7.8 per cent, of the 114 patients studied had anal ulcerations or anal contracture.

### ULCERATION IN LOWER PART OF THE BOWEL AFTER SHORT CIRCUITING OPERATIONS

On sigmoidoscopic examination of 4 patients 5.3 per cent of the group, 1 to 3 years after short

circuiting operations, ulcerations were found in the lower part of the bowel. These operative procedures consisted of some type of short circuiting operation, such as ileosigmoidostomy and resection of the diseased portion of the ileum. On sigmoidoscopic examination from 1 to 2 years later, ulceration of the mucosa of the bowel near the site of ileal anastomosis was observed. The ulcers were 2 to 3 centimeters in diameter, superficial, and had irregular margins. They were solitary in all but 1 case, in this case 2 ulcers were seen on sigmoidoscopic examination. Their presence probably indicates return of the infectious process.

#### SUMMARY

One hundred fourteen consecutive patients with regional ileitis, all of whom underwent sigmoidoscopic examination, were studied to determine the anorectal manifestations of the disease. Thirty six patients, 31.6 per cent, had an anal abscess or anal fistula or gave a history of having had an operation for anal fistula. The main complaint of 8 of these 36 patients was anal fistula, the regional ileitis remained undiscovered until a later date. In examination of 17.5 per cent of this group of 114 patients, an extrarectal mass was found. Anal ulceration, or a con-

tracted anal outlet, was found at examination of 7.8 per cent of the patients. Three and five-tenths per cent had ulceration of the lower part of the bowel after short circuiting operations and resection of the diseased portion of the bowel.

#### INFERENCES

1. An anal abscess or anal fistula is frequently the factor which will bring a patient with regional ileitis to his physician.

2. If the patient is a young adult with any vague intestinal disturbance, the presence of an anal fistula or the history of an abscess or fistula should lead the clinician to investigate the small bowel for regional ileitis.

3. Any patient who has an anal fistula is entitled to a proctoscopic examination and, if abdominal symptoms coexist, to roentgenologic examination of the large and small intestine.

4. Regional ileitis should be considered as a possible cause of any extrarectal mass of undetermined cause.

#### REFERENCES

1. BUIE, L. A., JACKMAN, R. J., and VICKERS, P. M. *J Am M Ass*, 1941, 117: 167-169.
2. PENNER, ABRAHAM, and CROHN, B. B. *Ann Surg* 1938, 108: 867-873.

# THE EFFECT OF ESTROGENIC SUBSTANCE UPON UTERINE MOTILITY DURING LATE PREGNANCY

An Analysis of 153 Observations Made with the Lóránd Tocograph

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HOW to treat primary uterine inertia satisfactorily continues to be a pressing obstetrical problem. Because the commonly used oxytocic drugs frequently fail to remedy this condition, the study of any substance which has been shown to influence uterine motility would seem to have merit.

Animal experiments have demonstrated that estrogenic material will increase uterine activity and likewise render the pregnant uterus more responsive to the oxytocic principle of the posterior pituitary gland (6). The human uterus also reacts to the administration of estrogens. Patients suffering from gonorrheal vaginitis have experienced uterine cramps following treatment with this material (6); furthermore, obstetricians have reported improved labor following the administration of estrogenic substance to patients suffering from primary inertia (3).

One observer and 6 external hysterography has recorded the effect of estrogenic substance upon the human uterus during labor (7). He found that the drug was inconsistent in its action. The number of his observations was small, and his evidence that the material had an oxytocic effect was not entirely convincing.

Such observations as these—based upon either subjective uncontrolled, or inconclusive evidence—suggested a reinvestigation of the oxytocic property of estrogenic substance. For our study it was considered advisable to utilize patients who were not in labor in order to have a test organ which was relatively quiescent.

## MATERIALS AND METHODS

Thirty-nine women residing in two Philadelphia maternity homes were studied. Their uterine activity and reactivity were registered with a Lóránd tocograph (4, 5). With this instrument we secured 153 sets of observations upon the effect of estrogenic substance on the pregnant uterus, and 19 sets of control observations. All

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Assisted in part by grant from Ciba Pharmaceutical Products, Inc.

of these were made between the 33d week of pregnancy and labor. A set of observations consisted of 3 tocographic tracings of given individual on the same day.

Estrogenic material was administered in sesame oil. Two preparations of  $\alpha$ -estradiol were used. One form, the dipropionic ester of estradiol, was administered in a dose of either 0.5 milligram or 1 milligram; the other form, the nonesterified material (i.e., plain  $\alpha$ -estradiol) was given in a dose of 3.54 milligram, which is the molecular equivalent of a dose of 0.5 milligram of estradiol dipropionate.

Eight control observations followed the administration of sesame oil alone and 11 were made upon patients who received neither sesame oil nor estrogenic substance.

The observations were carried out in the following manner: The patient rested upon her bed for 10 minutes. The tocograph was then placed upon her abdomen. Spontaneous uterine activity was recorded for the following 15 minutes. The tocograph was then removed and the drug was administered. Each dose, 1 or 2 cubic centimeter of sesame oil, was injected intramuscularly in the upper arm. After a predetermined interval of time had elapsed, the tocograph was replaced and a 30 minute record of uterine reactivity was made.

The effectiveness of the treatment was measured in terms of its ability to increase either (1) the tonus of the uterus or (2) the frequency, strength, duration, or rhythmicity of the inter-

TABLE I.—INFLUENCE OF DURATION OF PREGNANCY UPON INCIDENCE OF UTERINE RESPONSE TO ESTROGENIC SUBSTANCE

Duration of pregnancy	Number	Observations showing response to treatment	Per cent
Weeks			
5-28	3	0	0
29-32	8	0	0
33-36	35	20	57
37-40	8	40	50
Total	53	60	60

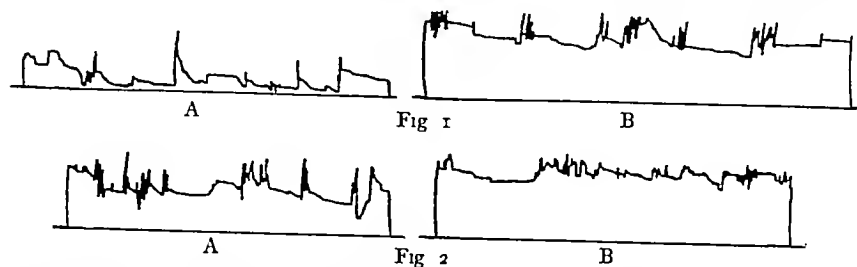


Fig 1 Tracing of uterine motility of patient I M secured 6 days before labor. Dose of 0.5 milligram of a-estradiol dipropionate administered at end of tracing A. Note in tracing B that the uterine tonus is very much higher than in tracing A. Vertical strokes in tracing B register active fetal movement. Break between A and B indicates  $2\frac{1}{4}$  hour interval.

Fig 2 Tracing of patient I M (Fig 1) 4 days before labor. Dose of 0.5 milligram of a-estradiol dipropionate administered at end of tracing A. Note the increase in tonus in tracing B, following treatment. This increase occurred although the original tonus was higher than it was 2 days previously (tracing A, Fig 1). Break in tracing indicates  $2\frac{1}{4}$  hour interval.

mittent contractions. The results are presented graphically and statistically.

### RESULTS

Of the 153 sets of observations upon the effect of both compounds, 62, or 40 per cent, registered an increase, irrespective of dosage, in one or more characteristics of uterine activity. The a-estradiol dipropionate was administered 112 times in a dose of 0.5 milligram. In 45, or 40 per cent, instances a positive effect was recorded. In 36 cases the a-estradiol dipropionate was administered in a dose of 1.0 milligram. In 15, or 41 per cent, instances a positive response was noted.

The plain a-estradiol was administered 5 times in a dose of 0.354 milligram. A positive response was observed twice, 40 per cent. Therefore, the incidence of uterine response to estrogenic substance appeared to be independent of the form in which the drug was given or its dose.

The 153 sets of observations dealing with the administration of both compounds are summarized in Table I, according to the duration of pregnancy at the time that the treatments were given.

No contractile response was observed prior to the 29th week of pregnancy. After the 28th week, the longer the duration of pregnancy, the larger was the number of responses, but at the very end of pregnancy, only about one-half of the tracings recorded a positive response.

The 153 sets of observations are summarized in Table II according to the interval between treatment and the time that observation of uterine reactivity was begun. The positive responses were observed with about equal frequency from 1 to 3 hours after treatment.

Table III records the character of the positive responses. The drug influenced both tonus and the intermittent contractions, the latter slightly more often than the former.

Table IV records the influence of the drug upon the character of the intermittent contractions. The magnitude of all characteristics was increased, especially that of frequency and of strength.

**Control observations.** The uterine motility of 19 control patients was recorded for a period of 15 minutes, followed by a second record of 20 minutes, at the end of 2 hours. Following their

TABLE II — INFLUENCE OF INTERVAL BETWEEN INJECTION AND OBSERVATION UPON INCIDENCE OF UTERINE RESPONSE TO ESTROGENIC SUBSTANCE

Interval between injection and observation	Observations		
	Number	Showing responses	Per cent
Hours			
Under 1			
1	4	1	25
2	32	14	44
$2\frac{1}{2}$	43	18	42
3	27	11	41
4	31	13	42
5	10	2	20
6	5	3	60
	1	0	0
Total	153	62	—

TABLE III — TYPE OF UTERINE RESPONSE TO ESTROGENIC SUBSTANCE

Type of response	Observations		
	Number	Showing responses	Per cent
		Number	
Contractions	153	51	33
Tonus	153	36	23
Contractions affected and not tonus	153	26	17
Tonus affected and not contractions	153	11	7
Both tonus and contractions	153	25	16

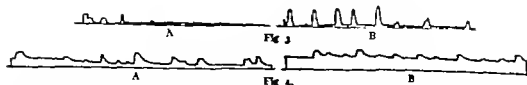


Fig. 3. Tracing of uterine motility of patient G. J. secured 30 days before labor. Dose of 0.5 milligram of  $\alpha$ -estradiol dipropionate administered at end of tracing A. Note in tracing B an increase in the frequency and in the strength of the intermittent contractions. No accompanying increase in toms. Break between A and B indicates  $3\frac{1}{2}$  hour interval.

Fig. 4. Tracing of uterine motility of patient A. W. secured 8 days before labor. Dose of 5 milligrams of  $\alpha$ -estradiol dipropionate administered at end of tracing A. Tracing B notes both an increase in toms and an improvement in the rhythmicity of the intermittent contractions. Break in tracing between A and B indicates  $3\frac{1}{2}$  hour interval.

first tracings, 8 individuals received 1 cubic centimeter of sesame oil containing no estrogenic substance. The remaining 12 patients received no treatment of any kind. In neither group of observations did the second tracing show an increase in activity over that noted in the first tracing.

**Graphic observations.** Effect primarily upon toms. Patient I. M. supplied tracings 2, 243 A and B and 2, 247 A and B (Figs. 2 and 3). The tracings in Figure 2 were secured 6 days before labor. Immediately following tracing A the patient received 0.5 milligram of  $\alpha$ -estradiol dipropionate. Tracing B was started  $3\frac{1}{2}$  hours after treatment.

The tracings in Figure 3 were made 4 days before labor. The kind of drug, its dose, and the interval between treatment and observation were the same as for the tracings in Figure 2.

These two sets of observations indicate that an increase in toms followed treatment, with no appreciable coincident effect upon the character of the intermittent contractions. Increase in toms is indicated by elevation of the valley level of the intermittent contraction waves above the base line.

**Effect upon contractions.** Patient G. J. on the 30th day before labor received 0.5 milligram of  $\alpha$ -estradiol dipropionate immediately after tracing 2, 204 A was made (Fig. 3). Tracing B was begun  $3\frac{1}{2}$  hours after treatment. Note in the

second tracing the increase in activity and the change in the pattern of the contractions, which occurred without any appreciable alteration in toms.

**Effect upon toms and contractions.** Patient A. W. on the 9th day before labor received 0.5 milligram of  $\alpha$ -estradiol dipropionate immediately after tracing 2, 123-A was made (Fig. 4). Tracing B was begun 3 hours after treatment. Note in the second tracing the concurrent increase in toms and in rhythmicity of the intermittent contractions.

#### EVALUATION OF STUDY

One value of the present study lies in the fact that it utilized an objective method for recording uterine reactivity. A second value lies in the fact that the tocograph supplies a permanent record which makes it possible to measure the effect of an oxytocic drug quantitatively as well as qualitatively. The third value lies in the fact that our observations were made upon patients who were not in labor. By using them, we eliminated the element of strong and variable contractions characteristic of labor, the presence of which has a tendency to overshadow the necessarily weaker contractions induced by an oxytocic drug.

Our observations confirm those of others, namely, that estrogenic substance has an oxytocic effect upon the pregnant uterus. They indicate further that uterine reactivity to the drug is variable both qualitatively and quantitatively, and that the incidence of response increases as pregnancy advances. Our observations suggest that continued study of estrogenic substance is necessary before its use in the treatment of primary inertia can be placed on a scientific basis.

#### SUMMARY

1. Estrogenic substance in the form of  $\alpha$ -estradiol or  $\alpha$ -estradiol dipropionate was administered

TABLE IV.—INFLUENCE OF ESTROGENIC SUBSTANCE UPON INTERMITTENT UTERINE CONTRACTIONS

Characteristic of contractions	Observations showing response*		
	No. obs.	No. unres.	Per cent.
Frequency	8	45	18
Strength	57	43	80
Duration	5	35	74
Rhythmicity	57	23	64

\*Response represented by an increase of the characteristic

intramuscularly to a series of women who were more than 23 weeks pregnant but not in labor. Uterine activity and reactivity were registered with a Lóránd tocograph before and after treatment.

2 The estrogenic substance was variable in its oxytocic effect. No reaction occurred prior to the 29th week of pregnancy. After that time, the number of patients who responded increased progressively as pregnancy advanced. The estrogenic substance increased both uterine tonus and the various characteristics of the uterine con-

tractions, but the nature and degree of the response was unpredictable.

#### REFERENCES

- 1 ABARBANEL, A. R. Surg Gyn Obst, 1941, 73 257-262
- 2 EMBREY, M. P. J Obst Gyn Brit Empire, 1940, 47 371-390
- 3 JEFFCOATE, T. N. A. J Obst Gyn Brit Empire, 1938, 45 893-917
- 4 LÓRÁND, S. (LOEWI) Mschr Geburtsh Gyn, 1936, 103 137-145
- 5 MURPHY, D. P. Surg Gyn Obst, 1941, 73 681-685
- 6 REYNOLDS, S. R. M. Physiology of the Uterus. New York: Paul B Hoeber, 1939

## PAPILLARY CYSTADENOMA LYMPHOMATOSUM OF THE PAROTID GLAND

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A RARE tumor within the substance of salivary glands has been recognized and reported frequently enough within the past 20 years to be known as a distinct pathological entity, although theories of its origin are by no means of uniform accord. The neoplasm has been called adenolymphoma (Jaffe), oncocytoma (Hamperl, Jaffe), and papillary cystadenoma lymphomatosum (Warthin), the latter term being most commonly used at present.

The first case reported was that of Hildebrandt (Freshman and Kurland) in 1898, the author considering the tumor to be of branchiogenic origin. It is highly probable that numerous cervical masses considered branchiogenic cysts have actually been of the type herein reviewed. Warthin, in 1929, reported only 2 cases from several hundred thousand surgical specimens. In 1932, Jaffe had found 21 cases in the literature, Carmichael, Davie, and Stewart, by 1935, collected 26 reported cases and added 8 coming under their own observation, Harris, 1937, reviewed 41 cases, adding 2 of his own, Freshman and Kurland, the following year, stated that they had collected 54 known cases and added another of their own, Tuta and Apfelbach have recently added 1 more, and Plaut, in July, 1942, summarizes 48 cases in the literature and adds 19 more, bringing the total reported to 67.

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The tumor, itself, is a well encapsulated structure in salivary tissue, usually the parotid, although less frequently the submaxillary, sublingual, or buccal glands. A firm fibrous capsule separates it from the gland itself. The nodular mass is round, oval, coarsely lobulated, or bosselated and is moderately firm but cuts with ease, revealing a cut surface smooth or finely granular with numerous small cystic spaces. These cysts contain a thin serous, milky, or mucilaginous fluid often bearing a fine precipitate.

Histologically, the structure is almost invariably of a well differentiated type, usually quite benign, only 2 of the reported cases showing malignant change. The numerous cystic spaces are lined by two or three layers of pseudostratified columnar epithelium which may be ciliated and thrown up into many broad based branching papillae. In other cases the luminal epithelial layer may be tall, columnar, and nonciliated, while the basilar layer is cuboidal. The stroma consists of a delicate reticulum, sometimes collagenous, in which there are numerous closely packed lymphocytes or follicles with large germinal centers. Examination of the cyst fluid reveals a thick homogeneous substance bearing lymphocytes, desquamated epithelial cells, fat globules, and occasional corpora amylacea.

The multiple theories as to the origin of these unusual growths have been well reviewed by Kraissl and Stout, Freshman and Kurland, and





Fig. 1. Case 1. The cystic spaces are lined by double row of epithelium supported by lymphoid stroma. The spaces are seen to contain granular substance bearing few lymphocytes. X60.

Oden. The majority of earlier authors and many still today consider the cyst of branchiogenic origin. Another popularly accepted belief is the blending of lymphoid tissue of the preauricular node with a parotid lobule, the resulting mixture being separate from the parotid, itself. Warthin postulated a heterotopia or distopia of pharyngeal endoderm, or about the parotid the cells most closely resembling mucosa of the cartilaginous portion of the eustachian tube. Harris speaks of heterotopic salivary gland epithelium in lymphoid tissue. Other theories may be enumerated briefly: (1) failure of extrusion of lymphoid follicles; (2) development of normal salivary tissue; (3) misplaced thymic nodule; (4) ectopic tonsilla; inclusion of pharyngeal ectoderm of third and fourth branchial pouch; (5) metaplasia of endothelium of lymph vessels or lymphoid embryonic rests; (6) failure of remnants of undifferentiated salivary tissue to fuse with the ductile system; (7) orbital inclusion, an embryological epithelial structure the fate of which is unknown in man; and (8) from oncocytes, peculiar epithelial cells of parotid ducts or parenchyma developing in late life with granular character to the cytoplasm, and with dense, hyperchromatic, and often indented nuclei placed near the lumen.

Papillary cystadenoma lymphomatosa occurs chiefly in men of the 5th and 6th decades. However, the youngest case reported was 35 years, and the oldest, 92. The occurrence according to sex shows a preponderance of males over females in the ratio of 6 to 1. The parotid is involved considerably more frequently than the other true

ture the tumor is seldom showing about equal incidence. The tumor involves most often the lower pole of the parotid, is slow growing, and usually painless unless growth is rapid, and is not attached to the skin but to the deep structures. According to Carmichael, Davis, and Stewart, the average preoperative duration is 6 years. The growth may vary from 2 to 10 centimeters in diameter. Fungation and necration are rare. As the tumor is well encapsulated, it is usually easy to remove. Recurrence is quite rare and irradiation therapy is of no value.

#### CASE REPORTS

CASE 1. J. M., 51, male, aged 45 years, was seen in the out-patient department of the University of Kansas Hospitals, May 16, 1934, complaining of right lower jaw. Incidentally he mentioned painless lump of 30 years duration on his forehead above the eyebrow. It had grown slowly until 4 years ago, increasing in size more rapidly since, but still painless. Within the past 8 months he had a small, hard, nontender mass in his neck just behind the angle of the left jaw.

Examination revealed a firm, lobulated, nontender growth on the left side of the forehead, 3 centimeters in diameter and 1 centimeter in thickness. It was freely movable, not attached to skin or deep structure. Posterior to the angle of the jaw, on the left and at the upper of the lower pole of the parotid, there was a firm, rounded, nontender nodule 3 centimeters in diameter, multilobulated to the skin, but barely adherent to deep structures.

Considering the growth on the forehead a fibrous tumor, cyst possibly having undergone epitheliomatous change, and the cervical nodule, made probably benign metastatic carcinoma, both were excised June 7, 1934, under local anesthesia. No difficulty as excision except that the cervical mass, as enclosed in a firm fibrous capsule, clearly adherent to the parotid capsule. Wounds were healed by days.

The pathological report came as follows: On gross inspection, the specimen measured 35 by 7 by 4 millimeters and was covered by fibrous capsule 1 firm area 8 millimeters in diameter as present but on periphery the node like mass revealed brownish-bite cellular structure bearing numerous cystic areas, the largest measuring 4 millimeters in diameter. These spaces contained an amorphous substance having the consistency of cartilage (1) making hardened.

Microscopical study revealed glandular and papillary papillary structure back as lined by layer of tall cylindrical epithelium. In places, this epithelium is cuboidal and now and then appeared to be of an embryonic type. The stroma supports the epithelium as of the lymphoid type and numerous follicles might be seen, some showing germinal centers. Some of the cyst like spaces contained mucinous secretions as recognized. Aids in other dequarated epithelial cells and clear staining vacuoles were seen. At the periphery of this growth and directly contiguous to it there was some salivary tissue with small ductal spaces lined by cuboidal epithelium. Islands of fat cells were scattered throughout the salivary tissue.

The growth removed from the scalp was typical fibrous tumor with areas of osseous metaplasia. Diagnosis: papillary adenocarcinoma lymphomatosa of salivary gland, probably parotid, fibrous tumor of scalp. Case 2. R. H., 61, male, aged 65 years, was admitted to the University of Kansas Hospitals, August 1, 1930, on the service of Dr. T. G. Orr. He stated that 6



Fig 2 Case 4 The papillary projections of epithelium into cystic lumina. The double row of epithelial cells is clearly demonstrated and the lymphoid stroma is definite.  $\times 110$

weeks before, while shaving he noticed a small "kernel" just in front of his left ear. It caused him no inconvenience or pain and had enlarged only slightly during the 6 weeks before admission.

On examination, a small tumor, 1.5 by 1 centimeter, was palpable just anterior to the left external auditory canal and extending slightly behind the ascending ramus of the mandible. It was firm, nontender, and movable on all surfaces except deep over the parotid capsule. Clinical diagnosis: parotid tumor.

The mass was excised under local anesthesia, August 7, 1940, without difficulty. It was well encapsulated and deep within the substance of the parotid extending down behind the angle of the jaw in the region of the facial nerve, which was not disturbed.

Grossly, the specimen was spherical, measuring 2.5 by 1.5 centimeters. It was gray in color with numerous fatty tags on the surface. The mass cut with ease and on section the tumor was seen to be cystic with a wall of 1 to 2 millimeters in thickness. The contained fluid was straw-colored. Portions of the inner lining were smooth and glistening, other portions were irregular containing small papillary granulations which extended inward 1 to 2 millimeters.

Section through the wall of the cyst showed a thin fibrous capsule and an inner lining of epithelial structure with papillary processes extending into the lumen. The cells were of indefinite epithelial type and were supported by abundant lymphoid tissue which rested against some glandular duct-like spaces lined by cuboidal epithelium and supported by a small amount of fibrous stroma. An acute and chronic inflammatory reaction was noted in the lymphoid tissue. The sections gave the appearance of some embryonic remnant.

Diagnosis: papillary cystadenoma lymphomatousum of parotid gland.

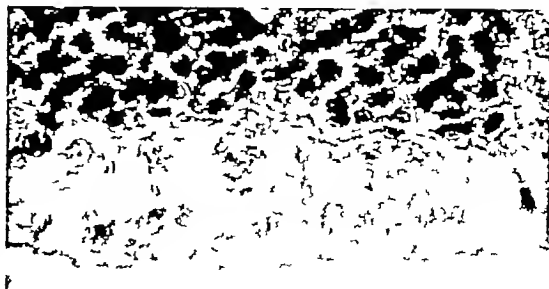


Fig 3 Case 4 Study of the epithelium shows the luminal columnar and basilar cuboidal layers. A suggestion of cilia may be seen along the luminal border. The basement membrane is fairly definite and lymphocytes in the stroma may be seen.  $\times 550$

CASE 3 R M G,<sup>1</sup> a white male, aged 28 years, was admitted March 22, 1937, to the service of Dr. William Ketchum at St. Joseph's Hospital, Kansas City, Missouri, with the chief complaint of weakness and fatigue, worse in the past year. For some time (exact duration not stated) he had had a small lump on the right side of the neck which varied in size and at times throbbed. Examination showed a mass, 3 by 2 centimeters, behind and below the angle of the right jaw fixed to the underlying tissues, but not to the skin. Pulsation was noted and attributed to the underlying vessels. The remainder of the examination, including laboratory procedures, was negative.

Grossly, the mass measured 3 by 2 by 1.5 centimeters and showed a rough fibrous capsule. When it was sectioned it exuded a creamy purulent material which was smeared and cultured, however, it showed no evidence of bacterial organisms.

The histological sections showed a papillary and cystic structure in which the trabeculae were made up of varying thicknesses of fibrous and lymphoid stroma which was covered over by a layer of cylindrical or pavement type of epithelial cells. In some places, the cells were tall columnar in type, while in others they were oval, round, or polyhedral and assumed more of a pavement characteristic, suggesting incompletely differentiated squamous cells. The

<sup>1</sup>Dr. Ketchum kindly permitted us to use this case and Dr. Russel Kerr, pathologist of St. Joseph's Hospital, furnished us with an abstract of his report.

lymphoid tissue as also variable in amount and in some fields actual germinal follicles could be seen. Areas of inflammatory reaction are present with an infiltration of polymorphonuclear leucocytes, some of which are eosinophilic. Desquamated epithelial cells and polymorphonuclear leucocytes could be seen within some of the cystic spaces.

**Diagnosis:** papillary cystadenoma lymphomatosum of the parotid gland.

**CASE 4.** A white female aged 65 years, as seen by Dr E. H. Dellinger of Los Angeles, New Mexico, in April, 1941. She complained of growth in the right side of her neck which had been present 3 years, growing slowly. The mass was located lateral to the upper pole of the thyroid on the right just beneath the deep cervical fascia. It seemed completely encapsulated and apparently had no connection with the thyroid itself. The mass was removed in its entirety.

The specimen consisted of several nodular pieces of tissue cysting together 30 grams and the largest measuring 6 centimeters in diameter. The external surface was smooth and resembled serous membrane, with some fibrous tags adherent to the capsule. The tissue was firm in consistency. Cut section revealed grayish tan mottled surface, granular and cystic in appearance. Its irregular foci of yellowish translucent substance. The granular tissue resembled thyroid gland with dilated follicles containing colloid material.

Microscopic examination showed lymphoid tissue supporting numerous irregular anastomosing glandular spaces lined by high, cylindrical epithelial cells with oval or round nuclei near the free edge. In most places, there was basal layer of cuboidal epithelium along with the marginal columnar cells, making double row resting on thin basement membrane. Some of the columnar cells were ciliated. The lumina of the cystic spaces contained granular homogeneous substance with an occasional desquamated epithelial cell or lymphocyte. Into the lumens of these glandular spaces, papillary projections of epithelium stood out. Numerous closely packed lymphocytes are present everywhere in the stroma and, in some places, typical germinal follicles are seen. Salivary glandular tissue was seen.

**Diagnosis:** papilliferous adenocystoma lymphomatosum, Not malignant.

With the 4 cases herein reported, 71 have now been described in the literature. These 4 have all been added within the past 5 years from the examination of approximately thirty thousand surgical pathology specimens examined by the pathology department of the University of Kansas School of Medicine and of St. Joseph's Hospital. Since it is only within the past few years that this tumor has been recognized as occurring in salivary gland tissue, doubtless many new cases will be added to the literature within the next few years instead of being forgotten when classified as branchiogenic cysts or embryonic rests of pharyngeal ectoderm.

The epithelium lining the cysts of the 4 cases reported varied somewhat. All showed the typical two layers of cells, the outer columnar and basilar cuboidal, but Cases 2 and 3 also, showed patchy areas where the epithelium was changing over into squamous type. Two of the cases showed ciliated columnar epithelium. Within 2 cases had cilia in the lumen of the cysts, but the great majority have not. Nothing to suggest malignancy was noted in our cases. While of a total of 7 now reported, only 2 cases have shown malignant change.

## REFERENCES

1. CARROSWILL, R. D. VIR, T. B., and STEIN, M. J. *J. Path. Bact. Lond.* 1935, 40, 69.
2. FREEMAN, W. A. W. and K. ELIAS, S. K. *Am. J. Clin. Path.* 1937, 8, 422.
3. HARRIS, P. W. *Am. J. Path.* 1937, 3, 81.
4. JONES, R. H. *Am. J. Cancer* 1932, 6, 43.
5. KRAUSE, C. J. and STOUT, A. J. *Arch. Surg.* 1933, 96, 483.
6. OBER, C. *Am. J. Surg.* 1933, 50, 37.
7. PLATT, J. A. *Ann. Surg.* 1932, 94, 843.
8. TAYLOR, C. and APPELBAUM, A. *Am. J. Surg.* 1932, 58, 304.
9. WARTER, A. S. *J. Cancer Res.* 1930, 3, 8.

Dr Dellinger kindly permitted us to use this case report.

# METASTATIC LESIONS OF THE STERNUM

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**T**UMORS involving the sternum are not common Heuer, in 1932, collected from the literature a total of only 38 cases in which the lesions were reported and described as tumors of the sternum In this series there were 19 primary sarcomas, 3 so called fibroid tumors, 3 primary cartilaginous tumors, 1 gumma, 1 chronic inflammatory lesion, and 6 metastatic lesions In the other cases in the series the tumor was not diagnosed Of the metastatic lesions, 2 were from carcinomas of the breast, 2 from hypernephromas, 1 was from a sarcoma of the breast, and 1 from a "malignant thyroid tumor" Low-Beer reported 6 cases in which there were destructive lesions of the sternum, in these 6 cases, 2 lesions were metastatic from a carcinoma of the thyroid, 1 was a metastatic lesion from a carcinoma of the breast, 1 was a round cell sarcoma, 1 was a syphilitic lesion, and 1 of the lesions was chronic osteomyelitis with sequestrum

Of 18 pulsating neoplasms of the sternum reported in the literature up to 1936, Crile concluded that 9 were probably metastatic hypernephromas and 9 were probably metastatic lesions from malignant adenomas of the thyroid Other cases of pulsating tumors of the sternum secondary to hypernephromas have been recorded by Roth and Davison and by Lewis In recent years, other cases of sternal tumors have been added to the literature, these include 2 cases of chondrosarcoma (1, 9), 1 gumma (4), 1 neurofibroma (3), 1 echinococcus cyst (11), and an osteomyelitic abscess (7)

In the files of the Mayo Clinic there are 14 cases of neoplastic involvement of the sternum 4 primary chondrosarcomas, 2 myeloblastic sarcomas, 1 endothelioma, and 7 metastatic tumors Of the 7 metastatic tumors, 1 is from a carcinoma of the breast, 1 from a carcinoma of the thyroid, 1 from a carcinoma of the stomach, 1 from a carcinoma of the rectum, 1 from a hypernephroma, and 2 are from a possible primary pulmonary malignant lesion It is with these last 2 cases that we are concerned in this report, since, to our knowledge, no similar cases have been recorded as yet in the literature

## REPORT OF CASES

**CASE 1** The patient, a railroad conductor aged 42 years, was seen at the clinic for the first time on September 22, 1941 He stated that 6 months prior to his coming to the clinic, following the extraction of 2 teeth, he had noticed a gradual onset of pain over the upper third of the sternum This pain would extend occasionally to the interscapular region and was aggravated by any active forceful movement of the arms Various medicines and hypodermic injections prescribed by his local physicians had been in effective in abating the pain, although the pain was lessened to some extent by taking 1 or 2 tablets of acetylsalicylic acid every 2 hours and by complete relaxation of the shoulder muscles The patient was not seeking compensation although he had been unable to work for 1 month He stated he would "go back to work tomorrow" if he could be rid of the pain in his chest He had lost 10 pounds (4.5 kgm) since the onset of his present illness

Physical examination gave essentially negative results except for considerable tenderness over the sternum at the level of the 3d and 4th costal cartilages There was no evidence of swelling, redness, or local elevation of temperature in this region Results of the flocculation test for syphilis were negative, the concentration of hemoglobin was 12.9 grams per 100 cubic centimeters of blood, leucocytes numbered 9,000, and erythrocytes 4,830,000 in each cubic millimeter of blood Several urinalyses showed albuminuria grade 1 (on the basis of 1 to 4, in which 1 designates the mildest and 4 the most severe condition), no sugar, an occasional erythrocyte and pyuria grade 2 (30 cells) A roentgenogram of the thorax, taken to show pulmonary detail, was reported as being negative Roentgenograms of the sternum, however, revealed a destructive lesion involving the body of the sternum with some sclerosis surrounding the lesion (Fig 1, a and b) From the appearance of the roentgenograms alone, a diagnosis of osteomyelitis of the sternum was made Roentgenograms of the cervical and thoracic portions of the spinal column were reported as being negative

It was deemed advisable to remove a specimen of sternal tissue for microscopic diagnosis At the time of operation, the periosteum of the sternum was found to be greatly thickened, there was no evidence of osteomyelitis no purulent exudate or abscess cavities were encountered Microscopic sections of the tissue removed presented the picture of an adenocarcinoma grade 4 (Broders' method), possibly metastatic from a primary pulmonary malignant lesion (Fig 2)

A course of roentgen therapy was given through four fields converging on the sternum with a moderate voltage technique (130 kilovolts) The total dose was 2,142 r measured in air

**CASE 2** A machinist aged 41 years, was admitted to the clinic on November 8, 1939 He stated that in February, 1939 he first had noticed the gradual onset of a constant dull pain behind the lower half of his sternum This pain became progressively worse with occasional extension to the interscapular region Coughing aggravated the pain compression of the chest by strapping with a towel gave some slight relief from pain The pain was not severe enough to keep the patient awake at night There had been no dyspnea, hemoptysis, chills, fever, loss of weight

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Fig. 1 Metastatic adenocarcinoma of the sternum in Case 1. a, left, posterolateral view and b, lateral view showing destructive lesion with surrounding sclerosis in the upper portion of the body of the sternum. This has the appearance of osteomyelitis rather than of metastatic malignant lesion.

calness, or shortness. The patient stated that he felt as though he had something behind the sternum that he could not cough up but his efforts to do so were ineffectual.

In 1937 one week after tonsillectomy the patient had had an attack of acute polyarthritides involving nearly all the joints except the fingers. The joints were red, tender and swollen. He was in bed for 3 months, had high fever and chills, and lost 30 pounds (13.6 kgm.). This condition recurred spontaneously about six apparent residual stiffness of 7 joints.

On physical examination there was tenderness over the middle third of the sternum. There was evidence of swelling, redness or increased warmth. Over the left side of the neck an cystic tumor of the scalp approximately 5 centimeters in diameter which had been present since birth, thus as believed to be an epidermoid.

Results of the urinalysis and of the flocculation test for syphilis were negative. The concentration of hemoglobin was 3.8 grams per 100 cubic centimeters of blood. Leucocytes numbered 1,000 in each cubic millimeter of blood. The sedimentation rate was 4 millimeters in 1 hour. T estimations of sputum gave negative results for the tubercle bacillus. Roentgenograms of the thorax were reported to show active tuberculosis in the upper lobe of the right lung. Roentgenograms of the skull did not show any involvement of the bone by the soft tissue mass in the occipital region. Roentgenograms of the sternum revealed an extensive destructive lesion of the body of the bone with some proliferative changes (Fig. 3, a and b). The roentgenologist believed that the lesion in the sternum was most likely neoplastic process.

Several small specimens of tissue were removed from the sternum for diagnosis. At operation it was noted that the lesion seemed to be productive of new bone. Macroscopic examination of specimen of tissue removed showed only brown hyperplasia, osteomyelitis with periostitis.

On November 3, 1939, one roentgen treatment given to the sternum with moderate dosage technique



Fig. 2 Specimen removed for biopsy from the sternum in Case 2. Note the large irregular neoplastic epithelial cells invading the connective tissue stroma and attempting to form glands.

(30 kilovolts) the dose being 6 measured in air. The lesion was treated as an inflammatory mass.

The patient returned 5 weeks later to have further roentgen therapy. It stated that four weeks after the first treatment he was almost completely free from pain. Five treatments had been given, gradual return of the pain. The roentgen treatment given to this case consisted of 10 roentgen beams with the same technical factors as used previously. The total dose being 45 measured in air.

The patient was seen again on January 8, 1940. He had not obtained much relief from the roentgen treatment. Examination of the sputum again gave negative results for fungi and for the tubercle bacillus, the sedimentation rate was 8 millimeters in 1 hour. The results of the first strength purified protein derivative, tuberculin test and of the agglutination test for the organisms of brucella were negative. Roentgenograms of the sternum showed the same extensive destruction of the body of the bone. No proliferative changes as seen in the previous roentgenograms (Fig. 3, a and b). Roentgenograms of the skull showed little change from those taken on first admission.

The patient died 4 1/2 hours on June 8, 1940. Autopsy was performed by the local physician, and portions of the various organs were sent to Dr. F. T. Bell at the University of Minnesota. Dr. Bell reported on the specimens as follows: "The lung shows adenocarcinoma, and the lower marrow of the sternum is almost entirely replaced by connective tissue. I am not sure here the primary growth is situated."

In both of these cases there was no palpable or demonstrable tumor mass about the sternum. The chief complaint in each instance was of a constant dull pain over the sternum, occasionally extending to the interscapular region and the roentgenogram in each case shows of a destructive lesion involving the sternal body. In the first case a benign lesion—chronic pyogenic osteomyelitis—was suspected but was disproved. In the second case the original diagnosis of neoplastic lesion of the sternum was not confirmed by biopsy but was proved at necropsy.

We realize how difficult it is to be certain that the neoplastic lesion of the sternum in these 2 cases was metastatic from a primary pulmonary adenocarcinoma. In Case 1 there was no demonstrable evidence of a primary lesion anywhere in the body, bronchoscopic examination was not performed. The highly malignant and anaplastic character of the cancer cells as seen in the microscopic sections of the specimen taken for biopsy also made it very difficult for the pathologist to state the origin of the tumor definitely, however, the morphological characteristics of the large, irregular epithelial cells, together with their abortive attempts to form acini, make a pathological picture which more closely resembles an adenocarcinoma of the lung than a similar tumor of any other organ.

In retrospect, it is a simple matter to presume that the "active pulmonary tuberculosis" which was diagnosed roentgenologically in Case 2 was in reality a primary carcinoma of the lung. However, the location of the lesion—in the periphery of the upper lobe of the right lung—and the appearance of the lesion in the roentgenogram did not warrant any diagnosis other than pulmonary tuberculosis. Obviously our biopsy of the sternal lesion in this case was not a satisfactory one, tissue representative of the underlying pathological changes was not included in the specimens of tissue removed for microscopic examination. This stresses the importance of securing an adequate biopsy material in every case of a destructive sternal lesion. In this case a second biopsy probably should have been performed, although the course of the disease would certainly not have been altered by an accurate antemortem diagnosis.

If biopsy reveals the presence of a metastatic malignant lesion within the sternum, it is obvious that surgical removal of this bone will neither cure the patient nor prolong his life. On the other hand, if the tumor, benign or malignant, has arisen primarily from the sternum and has not extended too widely, an attempt should be made to remove the lesion in its entirety. This has been done successfully in many cases. Adequate drainage is all that is necessary, as a rule, to heal chronic osteomyelitis with formation of abscess, occasionally it is necessary to remove a large portion of the infected bone. Antisyphilitic treatment is, of course, all that is necessary to cure the rarely encountered sternal gummas.



Fig 3 Metastatic adenocarcinoma of the sternum in Case 2 a, left, Anteroposterior view and, b, lateral view, showing an extensive destructive lesion of the entire body of the sternum with proliferative changes

#### SUMMARY

We have presented 2 cases of metastatic malignant lesions involving the sternum and arising possibly from primary pulmonary adenocarcinomas. We wish to stress the importance of taking roentgenograms of the sternum in all cases of sternal pain. If a destructive lesion of the sternum is seen in the roentgenogram, an adequate specimen for biopsy must be taken to determine, first, the benignancy or malignancy of the condition, and second, the feasibility of complete surgical extirpation.

#### REFERENCES

- 1 BRADSHAW, H. H., and CHODOFF, R. J. *Am J Surg*, 1940, 48: 685-687.
- 2 CRILE, GEORGE, JR. *Ann Surg*, 1936, 103: 199-209.
- 3 GOUGFROT and MEYER HEINE, A. *Bull Soc fr derm syph*, 1935, 42: 284-286.
- 4 HALBRON, P., LENORMAND, J., BENZAQUEN, L., and SPIRE WEILL. *Bull Soc méd hôp Paris*, 1933, 49: 1072-1074.
- 5 HUFER, G. J. *Ann Surg*, 1932, 96: 830-842.
- 6 LEWIS, THOMAS. *Brit Heart J*, 1940, 2: 260-262.
- 7 LITTLE, G. D. *Canad M Ass J*, 1936, 34: 185-186.
- 8 LOW BEER, ADALBERT. *Röntgenpraxis*, 1931, 3: 817-830.
- 9 ROBERG, O. T. JR. *Surg Gyn Obst.*, 1935, 61: 68-82.
- 10 ROTH, L. J., and DAVIDSON, H. B. *J Urol*, 1937, 37: 480-489.
- 11 SINBERG, S. E. *Radiology*, 1936, 27: 736-740.

# THE CARBON DIOXIDE SNOW ELECTROCAUTERY TECHNIQUE FOR OCCLUSION OF ARTERIES

## Suggested Application to Arteriovenous Angioma of the Brain

JUDAH EBIN, M.D. New York, New York

**I**n an earlier paper (5) a new technique for the occlusion of large venous channels for use in cases in which conventional methods are not adequate has been described. This involves the combined use of carbon dioxide snow and the electrocautery. The application of this procedure to the treatment of venous angioma of the brain has been suggested.

This technique has since been used on arterial vessels in the hope that it might be applied to the treatment of arteriovenous angioma of the brain. In this lesion communication between an artery and a vein has been established by a mass of abnormal vessels which replaces the normal capillary bed. These vessels may be arterial, venous, or both. Cushing and Bailey have described the arteriovenous angioma as a "fairly well circumscribed vascular area composed of manifold partly thinned and partly thickened vascular trunks forming an inextricable coil of dilated and sinuous vessels of varied caliber through which the arterial blood passes from enlarged entering arteries directly into one or more greatly dilated veins of exit usually with the production of an audible bruit. The lesion lies on the surface of the brain covered by arachnoid and may project deeply into it, in the shape of an inverted cone, butting on the ventricle. The vascular mass is most frequently encountered in the fields of the middle and posterior cerebral arteries and the artery of the corpus callosum. Increased vascularity of the scalp with large and pulsating arteries, hypertrophy of one or both carotids and even secondary cardiac hypertrophy are frequently met with. The changes in the cardiovascular system are secondary to increased blood volume which results from the shunting of arterial blood directly into venous channels.

The arterial supply of the lesion originates in surface vessels, although in the fully developed angioma the arteriovenous communication may be deep and thus not visible in the exposed operative field. Two types of arteriovenous angioma as

seen at operation may be distinguished. In the first both the arterial and venous portions of the mass are seen on the surface. The arterial channels are the entering arteries, or a communicating network partly or completely arterial, or both. Venous channels are communicating network partly or completely venous and terminal veins, or terminal veins alone. In the second, only the venous section of the mass is visible on the surface the arteries lying beneath it. The venous channels are a pure venous communicating network and terminal veins, or terminal veins alone. The presence of pulsation, thrill and arterial blood distinguishes this type from venous angioma. Histologically nodular overgrowths of the intima and telangiomatic nodules in the media have been noted. Hyaline degeneration may occur in the walls of the vessels in any of the coats.

The mode of origin of this lesion is in question. It is generally agreed that it is a congenital blood vessel malformation rather than a new growth. Some believe that it is arteriovenous at first but is not activated until middle life. Others think that it starts as venous angioma which is subsequently arterIALIZED, perhaps as the result of trauma. Finally, there are those who believe that it may originally be either venous or arteriovenous.

Present methods of therapy include radiation, carotid ligation, decompression, and direct surgical attack. Radiation has not resulted in cure although amelioration of symptoms and signs has been reported. Ligation of the carotid arteries has been of limited value. Butch and Aron are of the opinion that it should be used only as a last resort in advanced cases. In the presence of marked extracranial vascularity bilateral external carotid ligation has been done before osteoplastic craniotomy in order to reduce operative bleeding. Subtemporal decompression and the partial decompression afforded by osteoplastic flap are beneficial but only temporarily. Permanent relief does not result.

The principal danger in the surgical approach to this lesion is severe bleeding from fragile vessels. The ligature and the electrocautery has been used singly or together. Large vessels in

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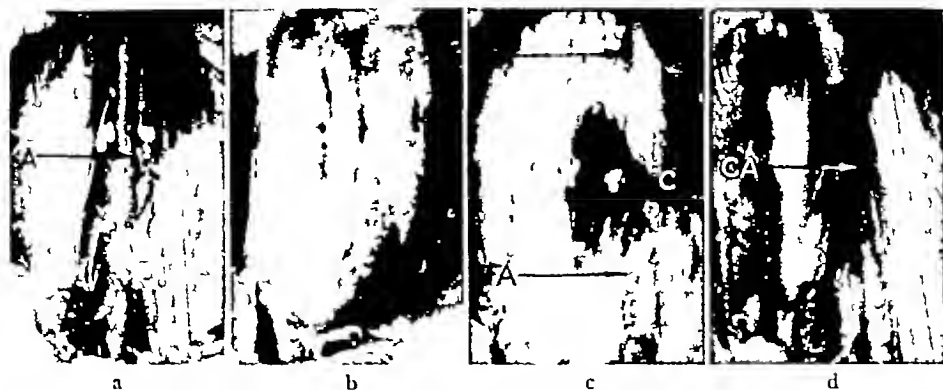


Fig 1. An artery, 4.5 millimeters in diameter frozen and coagulated. a Normal. b Frozen. c, Application of electrocautery to frozen vessel. C, electrocautery. F 1, frozen segment of vessel. Coagulated. C 1, Coagulated segment of vessel (Reduced one sixth)

been ligated followed by excision of the mass, or by electrocoagulation of the smaller channels, the electrocautery has also been used alone. These methods are hazardous, and severe hemorrhage has not infrequently resulted from their use.

Andrews reported a case in which an excellent result followed the injection of boiling water, homolateral external carotid ligation, and the application of hot soldering iron points. Dandy has presented a series of arteriovenous lesions. In one, very large Rolandic and Sylvian veins were exposed with a cluster of smaller veins about them. Pulsation of the mass and the presence of arterial blood indicated that there was an arterial communication. Ligatures were placed around the two large vessels, followed by almost immediate rupture of the venous mass between the two ties. In a second lesion, similar to the first, ligatures were placed about the veins, and the cortex was incised in an effort to find the arterial channels. These were located and ligated, following which the mass was removed. Cushing and Bailey reported a case of arteriovenous angioma of the right occipital lobe in which an attempt was made to coagulate the surface of the lesion. Each time the cautery was used a vessel which spurted arterial blood was torn. In Sachs' case the electrocautery was used successfully on the smaller vessels. It was then directed at one of the larger channels. Even though a low current was used, the vessel tore and an extremely severe hemorrhage resulted. Butsch and Adson reported a case in which the entering arteries were ligated and the vascular mass was coagulated with the electrocautery. A similar case was presented by Gardner. Arterial channels were ligated, following which the electrocautery was successfully used on the vascular mass. In Ray's case the electrocautery

was used on the angiomatous vessels. The caliber of the vascular channels treated in this manner was greatly diminished, but few vessels were completely occluded.

The carbon dioxide snow electrocautery technique has been used successfully to occlude 6 femoral arteries in dogs. The idea underlying this procedure is identical with that described for venous occlusion (5). Application of a block of carbon dioxide snow with moderate pressure empties and freezes the vessel, the interposed column of blood is eliminated. The apposed walls may then be coagulated by the electrocautery without tearing. The femoral artery in the dog is 4 to 5 millimeters in diameter. Arterial channels in the angiomatous mass of an arteriovenous angioma are seldom larger. As reported previously (5), the inferior vena cava in the cat and the dog have been occluded by the same procedure. These vessels are 6 and 13 millimeters in diameter, respectively. The venous channels of the angiomatous mass and the terminal veins are not of greater size. This procedure may be of use in the treatment of arteriovenous angioma of the brain. The entering arteries might be ligated, the arterial and venous portions of the angiomatous mass and the terminal veins might then be occluded in the manner described.

#### EQUIPMENT

A complete description of the equipment may be found in the preceding report (5). It includes blocks of carbon dioxide snow, cut with a hack saw, an Allis or curved clamp with rubber tubing on the prongs for handling the refrigerant, and the electrocautery. Both spark-gap and vacuum tube machines were employed in these experiments. These were the Leibel-Flarsheim portable Bovie electrosurgical unit and the Cameron cauteradio



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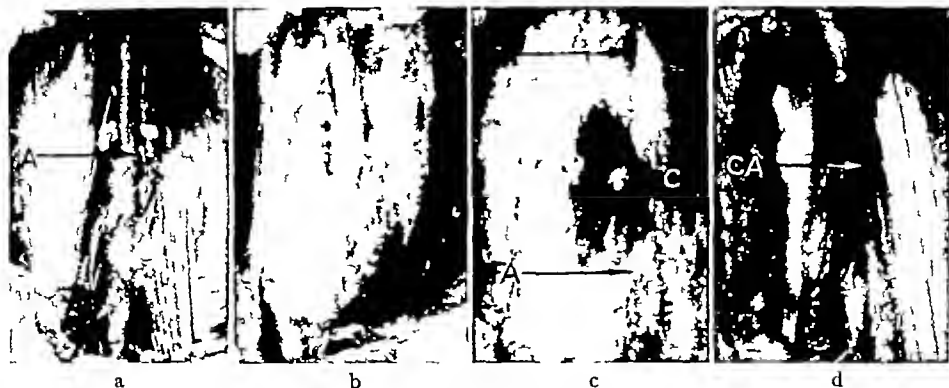


Fig 1 An artery, 4.5 millimeters in diameter, frozen and coagulated a, Normal A, Artery b, Frozen c, Application of electrocautery to frozen vessel C, electrocautery FA, frozen segment of vessel d, Coagulated CA, Coagulated segment of vessel (Reduced one sixth)

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Fig. 1. A bleeding artery 5 millimeters in diameter frozen and coagulated.  
a, Normal Vein 4 artery b, Bleeding T-Tear A blood Coagulated.  
c, Coagulated segment of artery (Reduced one-third)

model O respectively. The ball electrode measuring 5 millimeters in diameter was used on the vessels.

#### TECHNIQUE

The procedure is identical with that described for the occlusion of veins (5). To occlude segment of artery a block of carbon dioxide snow 6 by 1 by 2 centimeters is applied to it with moderate pressure; this also freezes lateral branches for a short distance before they enter the vessel. Lateral branches are frozen because it is possible for blood to enter the frozen strip through them by means of anastomoses with branches given off proximal to the frozen segment. After minute the refrigerator is removed. The electrocautery is then passed back and forth over the middle 3 centimeters of the frozen segment until coagulation and slight degree of carbonization have occurred. Because the walls of arteries are thicker than those of veins the current control is set at a slightly higher level for arteries. In the vacuum tube machine used in the spark-gap machine as compared with 5 and 10 to 35, respectively for veins.

During coagulation the two ends of the frozen segment and its branches are watched, and if blood appears in them coagulation is stopped and the procedure is repeated. Similarly, if blood appears in the lumen during coagulation while the ends and branches are still frozen coagulation is stopped. The end is thawed and the procedure is repeated. The presence of blood in the lumen is the result of incomplete emptying due to insufficient pressure in applying the refrigerator. The blood remaining is frozen and then thawed by the cautery.

If cauterization is carried too far or is continued in spite of the presence of blood in the lumen, the vessel wall may tear. In that event the segment is refrozen and the area about the tear is coagulated. If the exact location of the laceration is not known the artery is frozen for 15 seconds and then allowed to thaw until blood coalesces from the tear. The segment is then refrozen and the area about the laceration is coagulated.

#### PATHOLOGY

The effect of low temperature freezing has already been considered in detail (5). The conclusion reached was that low temperature freezing in itself does not injure tissue; that little damage follows refrigeration with dry ice is the result of pressure. The damage to brain tissue is superficial and negligible; veins, unaffected by the pressure involved, are not injured by the application of dry ice.

In order to study the long term effects of freezing an artery 1 centimeter distal to the femoral artery in a dog was frozen with moderate pressure for 1 minute. The animal was completely normal during the postoperative period. Examination at the end of 3 weeks showed that the vessel was patent and that there was no sterile reaction or infection. On microscopic examination the only change seen was a slight separation of the fibers of the outer layer of the adventitia.

In order to study the long term effects of freezing and coagulating an artery 1 centimeter distal to the femoral artery in a dog was occluded. After operation the animal was normal. After 3 weeks the vessel was re-exposed and was found to be still occluded. Neither rupture nor canalization had

occurred. No evidence of sterile reaction or infection was seen. On cross section the lumen was seen to be completely obliterated. Microscopic examination showed that the vessel wall in all its layers had a hyaline appearance as a result of coagulation.

#### SUMMARY

The carbon dioxide snow electrocautery technique produces permanent closure of both arteries and veins. The procedure is such as to do little damage to adjacent brain tissue. Application of this method to the treatment of arteriovenous angioma of the brain is suggested.

#### REFERENCES

- 1 ANDREWS, L. W. Surg Clin Chicago, 1917, 1: 965-969.
- 2 BUTSCH, W. L. and ANDSON, A. W. Surg Clin N America, 1935, 15: 1317-1326.
- 3 CUSHING, H., and BARRY, P. Tumors Arising from the Blood Vessels of the Brain. Springfield: Charles C. Thomas, 1928.
- 4 DANDY, W. I. Arch Surg, 1928, 17: 190-243.
- 5 LUBIN, J. Surg Gyn Obst, 1943, 76: 43.
- 6 GARDNER, W. J. Surg Clin N America, 1936, 16: 1019-1030.
- 7 RAY, BRONSON S. Surg Gyn Obst, 1941, 73: 615-648.
- 8 SACHS, I. Diagnosis and Treatment of Brain Tumors. St. Louis: The C. V. Mosby Co., 1931.

## TOTAL PNEUMONECTOMY

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NINE years have passed since there appeared the first report of a successful total pneumonectomy. Since that time the operation has been performed by a large number of surgeons, and the percentage of successful results has been steadily increasing. Yet all too often the general practitioner still considers the operation as too hazardous to contemplate. This idea frequently results in such delay in getting the patient to a thoracic surgeon that an operation may no longer be feasible. On the other hand, it has been found that if a total pneumonectomy is done upon patients who are in relatively good condition and are suffering from no other organic disease the mortality will be reasonably low.

The conditions which commonly require total pneumonectomy are bronchogenic carcinoma and extensive unilateral suppurative disease. The latter is usually bronchiectasis but may be multiple lung abscesses. Pneumonectomy may occasionally be justifiable for pulmonary tuberculosis.

### DIAGNOSIS

The early diagnosis of bronchogenic carcinoma depends largely upon the physician having a high index of suspicion. The common picture is that of a man in middle life or over who has a persistent cough of few weeks duration. The expectoration of some bloody sputum is highly suggestive. Pain in the chest and loss of weight are usually fairly late signs. It is believed, therefore, that every middle aged person who has a unexplained cough lasting 4 weeks or longer should be examined by x-ray and bronchoscope so that a diagnosis of bronchogenic carcinoma may be made early before the late signs of pain and weight loss appear.

Occasionally an early carcinoma may produce some bronchial obstruction with resulting atelectasis. Infection in the atelectatic area makes the patient ill and causes weight loss. The extension of the infection to the pleura causes pain. Thus the patient may have the late signs of bronchogenic carcinoma and yet have a localized operable lesion.

A large majority of bronchogenic carcinomas are within reach of the bronchoscope. Thus tumor may be removed and a positive diagnosis made by microscopy. When the tumor is in the periphery of the lung and cannot be reached by bronchoscopy, aspiration biopsy frequently will reveal a positive diagnosis. It is felt, however, that, if the x-ray appearance suggests carcinoma, an exploratory thoracotomy should be done even though a positive preoperative diagnosis is not made. Tumors situated in the periphery of the lung frequently produce no symptoms until secondary infection occurs. Occasionally there may be mediastinal metastasis before there is a simple sign or symptom. In such cases an early diagnosis is an impossibility unless the tumor is found at a examination made for some other reason. (This was the situation in Case 15.)

Bronchiectasis presents the problem of a complete diagnosis rather than an early one. A patient may have had the disease for years, bringing up large amounts of sputum, and because of this be set aside by his physician as a hopeless pulmonary cripple. On the other hand, careful bronchoscopic observations with complete bronchograms may reveal that the disease is entirely unilateral. If the entire lung is involved on one side and the other is free of disease pneumonectomy offers complete cure. Even when there is some bronchiectasis on the other side pneumonectomy may often be justified since the patient may be greatly improved although not completely cured.

Multiple lung abscesses carry a high mortality by any method of treatment. In the event that only one lung is involved, pneumonectomy offers the greatest chance of cure. It should be resorted to as soon as it becomes apparent that the disease cannot be brought under control by simple drainage.

A complete diagnosis of a patient who is a candidate for pneumonectomy for any reason involves the exclusion of other organic disease. The most important is heart disease since there can be no doubt that the heart is put to a severe test during the course of a pneumonectomy. It is important that one be aware of its condition before considering operation. If the patient has severe cardiac disease the idea of pneumonectomy has probably best be abandoned.

## PREOPERATIVE PREPARATION

When a total pneumonectomy is to be done for suppurative disease of the lung it is important that the good lung be as free of infection as possible. Repeated bronchoscopic aspirations and postural drainages may greatly improve the local condition and also the patient's general condition. The bronchoscopist must be the judge of when the good lung is sufficiently free of inflammation to go ahead with the operative procedure. Troublesome secretion during the postoperative period may result in atelectasis and bronchopneumonia. For this reason most patients are subjected to bronchoscopic aspiration a few hours before operation to decrease the possibility of a spill over during the operative period.

The usual patient with carcinoma does not have enough sputum to make it a major problem, so that very little preoperative preparation is necessary. However, the patient who has infection behind an obstructing carcinoma presents more of a problem. The bronchoscopist should attempt to free the obstruction to allow drainage of the infected area. If the patient's fever subsides, certainly his chances of surviving a pneumonectomy are increased. In the event that satisfactory drainage cannot be accomplished one must accept the increased risk of operation in the presence of acute infection or abandon the patient to his well known fate.

It is the custom of a number of surgeons to prepare the patient for pneumonectomy by a preliminary pneumothorax. This is done with the idea of getting the patient accustomed to the changed physiology. In the reported series it was found that pneumothorax was impossible in a number of cases first tried. These patients did well in spite of it so that preoperative pneumothorax was given up thereafter. We are not convinced that it is a helpful procedure.

For the last 2 years it has been our custom to use sulfonamide therapy for at least 24 hours before operation.

## ANESTHESIA

The thoracic surgeon asks two things of his anesthetists other than keeping the patient asleep, namely, providing adequate aeration and keeping the bronchial tree free of secretions. It is believed that this can be accomplished most satisfactorily by means of an intratracheal tube. The anesthetist can then insure adequate aeration and be constantly available to aspirate any secretion which may escape from the diseased lung into the trachea or bronchus during the surgical manipulation.

Whether the anesthetist takes over the patient's respirations entirely is a matter of personal preference. This has usually been done in this series. In several instances the patient did not have a spontaneous respiration for more than 2 hours. In none of these patients have any deleterious effects been observed as the results of this procedure. At times the absence of respiratory movements has been greatly appreciated by the operator.

## OPERATIVE TECHNIQUE

When an operation is being carried out in the neighborhood of so many vital structures, it is extremely important that one should have a satisfactory visualization of the operative field. Blind dissection should be avoided whenever possible. The Crafoord incision, removing the major portion of the fifth rib affords an excellent exposure. With this incision the mediastinal structures can be approached either from front or back, and parietal adhesions over almost any portion of the lung can be cut under direct vision. As the experience of the operator increases perhaps he can work safely through a smaller incision. An incision in the fourth or fifth interspace extending from the posterior axillary line to the midline anteriorly has proved to be quite satisfactory in recent cases. One or two costal cartilages may be cut anteriorly if necessary to give adequate exposure over the apex of the lung. This incision is especially valuable in the patient with suppurative disease with considerable purulent sputum. It is felt that such patients should be placed flat on their backs on the operating table to minimize the spill over of secretion from the diseased lung into the trachea. The anterior incision in the third interspace has been found to be unsatisfactory if there are extensive adhesions present, especially to the diaphragm.

The individual ligation of the great vessels and the separate closure of the main stem bronchus have now been universally adopted, while mass ligation and the multiple suture methods using a lung tourniquet have been abandoned in most clinics. Either heavy silk or catgut ligatures may be used on the great vessels. The usual custom is to place four ligatures on a great vessel, the middle two being suture ties. These two should be separated sufficiently so that when the vessel is cut between them there is a cuff of about  $\frac{1}{2}$  centimeter on either side. If this is impossible the sacrifice should be made on the pulmonary side which may be reinforced with a large hemostat.

Most surgeons close the main stem bronchus by the method described by Rienhoff (2) or

some variation of it. By this method the posterior wall of the bronchus is sutured to the anterior wall by three rows of interrupted silk sutures. Regardless of the method of closure of the bronchus it has been observed in this series that when there was so much infection present that the mediastinal pleura was left open, a temporary bronchial fistula has always followed. On the other hand, when the mediastinal pleura has been tightly closed, a bronchial fistula has never been recognized. It is of considerable interest, therefore, that Flick who makes popular the closing of the mediastinal pleura but who closes the bronchus with a single silk tie has not had one bronchial fistula develop. The possibility suggests itself, therefore, that the closure of the mediastinal pleura is the important thing and that the bronchus stays closed only until the mediastinum is well walled off. This has been suggested in some of our patients by the expectoration of a little mucopurulent material although no bronchial fistula was recognized.

Whether the chest cavity should be closed with or without drainage depends upon the amount of infection present. If a drain is used it means that the patient will have an infected pleural cavity which usually must be collapsed by a subsequent thoracoplasty. If the chest is closed without drainage and no infection occurs, the period of convalescence will be greatly reduced. On the other hand, the recent work of Loogacre and Johansmann suggest that the emphysema resulting in the remaining lung if thoracoplasty is not done may reach a detrimental degree. It is our feeling, therefore, that in the young patient with bronchiectasis for whom a complete cure is expected, the chest should be drained for fear of infection and a thoracoplasty done to avert future trouble from emphysema. On the other hand, it is desirable to close the chest without drainage in the patient with carcinoma and thereby avoid the morbidity of the subsequent thoracoplasty. Such patient recedes that those operated upon for bronchiectasis and in addition have the constant threat of recurrence of the carcinoma. Therefore the period of convalescence should be made as short as possible.

Before the chest wound is closed the second to seventh intercostal nerves have been cut or crushed on several occasions. This may be done easily from the inside of the chest and gives the patient a painless wound during the postoperative period. It is believed that this procedure is especially helpful in elderly patients since it allows them to lie on the side operated upon and thereby avoid the dependent pulmonary congestion which is

often so troublesome in these cases. It also allows the patient to cough and is very helpful when postoperative secretion is present.

When the chest is closed without drainage 5 grams of sulfanilamide is placed in the pleural cavity.

#### POSTOPERATIVE CARE

One must expect to give these patients great deal of attention during the postoperative period. If the mortality rate is to be kept at a minimum. Of utmost importance is the maintenance of adequate aeration. The mediastinal structures must not be allowed to shift to the side not operated upon thereby compressing the remaining lung. The patient whose chest is closed without drainage should be examined at frequent intervals for deformation of the mediastinum. It may be suspected because of tachycardia or respiratory distress. It may be confirmed by feeling for a shift of the trachea in the neck or for a shift of the apex beat. A portable x-ray examination should be done in case of doubt. Fluid or air should be aspirated at intervals if necessary to maintain the mediastinum in the midline or somewhat over to the side operated upon.

The patient whose chest is closed with drainage should have a right drainage with constant suction of about 7 centimeters of water exerted in the pleural cavity. In this way the normal pressure relationships are maintained in the thorax. Over a period of days the mediastinal structures will gradually shift to the side operated upon. The pleural cavity may be reduced in size to 300 to 500 cubic centimeters by the shift of the mediastinum, and the elevation of the diaphragm after a period of about a month after pneumonectomy. This usually must be closed by thoracoplasty. However 3 patients in this group had sufficient mediastinal shift to close the entire cavity without thoracoplasty.

In the patient whose chest is closed without drainage the serum in the pleural cavity shrinks and contracts, producing considerable shift of the mediastinal structures toward the side operated upon. This change reaches its maximum in about 6 months.

The prevention of postoperative atelectasis in the remaining lung is of the utmost importance. It is essential, therefore, that a free airway be maintained and that a viscous or purulent material be coughed out. The foot of the bed is usually elevated and the patient turned on the side operated upon for 24 hours. This allows dependent drainage until the patient is well over his anesthetic. Pain was found to be a major problem

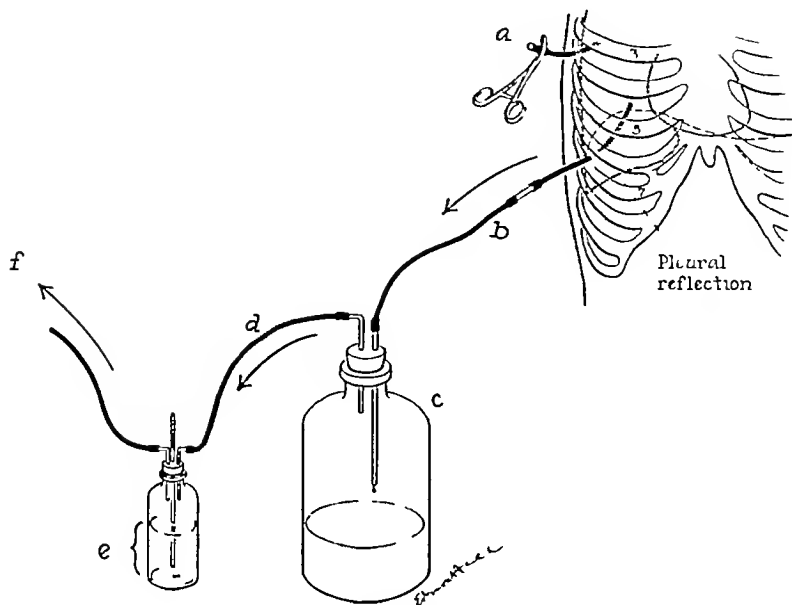


Fig 1 When the chest is drained after pneumonectomy the apparatus illustrated has been used to maintain negative pressure in the pleural cavity. Continuous water suction is applied at *f*. The amount of negative pressure in the chest is controlled by the depth of the glass tube below the water at *e*. By opening the tube at *a* intermittently, it is possible to maintain a pneumothorax rather than a serothorax and thereby avoid the danger of spill over into the other lung in the event that the bronchial stump should open.

in some of the patients in whom the intercostal nerves were not cut. It was necessary to find a happy medium in morphine dosage between giving so much morphine that the cough reflex was destroyed, and giving so little that the patient could not cough because of pain. On several occasions it was found necessary to give some morphine before the patient was sufficiently free of pain to cough up the mucus present in the trachea. On the other hand, sufficient morphine to make the patient comfortable, in at least one instance (Case 9), resulted in inadequate coughing and atelectasis of the right upper lobe on the third day after left pneumonectomy. Such a complication seriously threatens a patient's life and may be overcome only by the most energetic treatment.

It has been our experience, therefore, that these patients should be kept lying on the side operated upon, thereby giving good drainage of the remaining lung. The patient must be encouraged to take deep breaths to keep the lung clear and to cough out any mucus or purulent material which may be present. A painless wound due to crushed intercostal nerves has been found to give the patient a tremendous advantage in the execution of this plan.

Oxygen therapy has been used in the form of a nasal catheter for about 3 days after operation. The catheter is preferable to an oxygen tent because it makes nursing simpler and delivers a more constant supply of oxygen. The catheter should be removed and cleaned at frequent intervals. The oxygen tent is frequently used in the summer because of its cooling effect.

In 8 patients the wound was closed without drainage in the hope of shortening the convalescence, although the patients had infection in the lung and were febrile before operation. In spite of intensive drug therapy, infection occurred in all but 1 instance. When infection becomes evident drainage is imperative. This usually means that a subsequent thoracoplasty must be done to collapse the residual empyema cavity. It has been found advisable to wait at least a month after pneumonectomy before doing the thoracoplasty. It is desirable not to wait too long, however, as the pleura may become so thick and scarred that it does not collapse easily. In only 1 instance did infection occur in the serum pocket when the patient had no infection before operation. This case of infection was thought to be due to an inadequate closure of the mediastinal pleura.





Fig. 2. Case 9, 1 year after operation. This roentgenogram illustrates the late shift of the mediastinum when the chest is closed without drainage. The patient now has fibrothorax on the left. Note the barium in the esophagus. The shift of the mediastinum to the left, and elevation of the diaphragm. Also note the enlarged right lung extended long over to the left side.

When the chest has been closed without drainage death may occasionally occur by drowning due to the sudden opening of the bronchial stump with pouring of serum into the remaining lung. To avoid such an occurrence adequate closure of the mediastinal pleura is advocated. Moreover, the patient is constantly kept on the side operated upon and turned to the back only under supervision. In 10 of our patients whose chest had not been drained (Cases 0 and 4) the wound became infected and bronchial fistula occurred. In each instance this was recognized and the chest was drained before serious spill-over occurred, probably due to the patient's having been kept on the side operated upon.

If the patient's wound has been closed with a drain to which constant suction has been applied the chest cavity will still become filled with serum since there is an airtight connection between the tube and chest wall. Thus, if bronchial fistula should suddenly develop the patient may drown from serum leaking into the trachea. This would be most likely, of course, if he was

lying on the side not operated upon and less likely if he was lying on the side operated upon (this almost occurred in Case 11). The danger may be almost completely avoided, by placing a second tube in the chest through the back at intervals, which in turn allows the constant suction to remove the serum from the chest. Thus, a pneumothorax rather than a hydrothorax is maintained on the side operated upon.

#### MORTALITY

The mortality of total pneumonectomy has been steadily decreasing. It is obvious, however, that it must depend upon the type of patient operated upon and upon the thoroughness to detail in the preoperative and postoperative periods.

The mortality in the young individual should be low whether the operation is for carcinoma or suppurative disease. If, however, the suppurative disease is bilateral the risk is definitely increased. The mortality will of necessity remain fairly high in the group of elderly patients with carcinoma, primarily because of the associated diseases—most common of which is cardiovascular disease. The highest mortality will be found in the group of patients with infection superimposed upon carcinoma.

In the reported group of 20 total pneumonectomies, there was only 1 death. Thirteen of the patients were operated upon for carcinoma, 6 for bronchiectasis, and 1 for multiple lung abscesses. The low average age of the patients in this series undoubtedly is a major factor in the low operative mortality. Nevertheless, this group of patients certainly demonstrates that total pneumonectomy is a relatively safe procedure in the patient without associated complicating diseases.

#### END-RESULTS

All but 2 of these patients have been operated upon within the last 3 years so that end-results can hardly be reported. It can be said, however, that of the 6 patients operated upon for bronchiectasis having from 300 to 500 cubic centimeters of sputum daily before operation, 3 have apparently been cured and now have no cough and no evidence of bronchiectasis in the remaining lung. The other 3 have been greatly improved but still have occasional expectoration due to minimal bronchiectasis in the other lung. The patient with multiple lung abscesses has been completely cured and has no cough.

Of the 3 patients with bronchogenic carcinoma, 1 died of infection in the hospital, and 1 died of metastasis within a year. The other

gone more than 2 years without evidence of metastasis, 2 are well after 1 year and 6 for less than 1 year

### CASE REPORTS

CASE 1 W H, male, aged 17 years, in whom bronchiectasis was present for 11 years. The patient had repeated bronchoscopic treatments with symptomatic improvement. A bronchogram showed extensive bronchiectasis on the left. There was about 100 to 200 cubic centimeters of sputum daily. A left total pneumonectomy with drainage was done on October 7, 1937. The empyema closed with subsequent thoracoplasty. The patient is now well over 4 years with no cough.

CASE 2 F M, female, aged 30 years, was found to have bronchiectasis in 1926. A right thoracoplasty was done elsewhere in 1932. She was seen by us in 1937 when she had severe bronchiectasis on the right side. There was about 200 to 300 cubic centimeters of sputum daily. A right total pneumonectomy was done in three stages removing one lobe at a time by the multiple suture method. The last operation, on October 22, 1938. At her worst she coughs up 30 to 40 cubic centimeters of pus a day. A bronchial fistula was present for months but is now closed.

CASE 3 J K, male, aged 33 years, had coughed as long as he could remember. He had brought up 300 to 400 cubic centimeters of pus daily for the last 4 or 5 years. A bronchogram was normal on the right, but showed severe bronchiectasis on the left. A total left pneumonectomy with drainage was done on July 5, 1930. Thoracoplasty was performed on August 30, 1930. The patient has been entirely well with no cough since the operation.

CASE 4 E W, female, aged 26 years, had had productive cough for 10 years. There was hemoptysis at intervals for 3 to 4 years. The daily sputum was about 100 cubic centimeters. An incomplete bronchogram showed bronchiectasis in the left lower lobe. She was first seen by us in severe hemorrhage. A pneumothorax was required to stop it. Without the lung being allowed to re-expand, a left lower lobectomy was done by the multiple suture method on October 21, 1938. The patient still had about 50 cubic centimeters of sputum daily. A bronchogram showed bronchiectasis in the left upper lobe. Therefore, a left upper lobectomy was done on September 6, 1940 by individual ligation without drainage. The bronchus opened but the pleural space was walled off. A thoracoplasty was done after drainage of the cavity. She still has some cough from minimum bronchiectasis in the remaining lung.

CASE 5 M M, female, aged 36 years, had had a productive cough since a right sided pneumonia in January, 1939. A bronchogram showed severe bronchiectasis in the right upper and lower lobes. There were several severe hemorrhages. There were about 300 to 400 cubic centimeters of sputum daily. She weighed only 90 pounds having lost 70 pounds during her illness. A right total pneumonectomy with drainage was done on October 28, 1940, and a thoracoplasty on January 3, 1941. The wound is now closed. She is perfectly well with no cough and has regained her normal weight.

CASE 6 J P, male, aged 22 years, had had bronchiectasis for about 10 years. When first seen by us in 1939, he coughed up about 500 cubic centimeters of pus daily. Bronchogram showed extensive disease on the left and minimal bronchiectasis on the right. There were frequently periods of fever with a friction rub on the right. After almost 2 years' treatment the sputum was reduced to 200 cubic centimeters a day and the right lung was fairly clean. A left pneumonectomy without drainage was done October 6, 1941. The serum pocket became infected and required



Fig 3 Case 13, 1 year after operation. This roentgenogram illustrates the closure of a total empyema cavity without the aid of a thoracoplasty. Note barium in the esophagus showing the tremendous shift of the mediastinum which allowed the cavity to close. This case is exceptional in that a thoracoplasty must usually be done to close the cavity.

drainage. A thoracoplasty was done on January 19, 1942. The patient has very little cough and almost no sputum.

CASE 7 V D, female, aged 41 years, had epilepsy for 6 years. The productive cough started in June, 1939. There were several small hemorrhages. She was seen by us in October, 1939, and 2 abscesses were seen by x ray film in the right upper lobe. These were drained on November 1 and 11, 1939. A third abscess was found in the right middle lobe and drained February 9, 1940. A fourth abscess was found in the right lower lobe and drained on April 17, 1940. The patient continued to be febrile and a fifth abscess was seen by x ray film. Therefore, a total right pneumonectomy with drainage was done on June 10, 1940. A thoracoplasty was done on September 17, 1940. The patient is now well with no cough. She still has a small draining sinus.

CASE 8 C L, male, aged 42 years, had had 3 bouts of fever and pain in the left chest, diagnosed as pneumonia, since January, 1936. He was seen by us in January, 1939 with complete atelectasis and infection of the left lung due to a tumor of the left bronchus. He was given x ray treatment. A bronchoscopic biopsy of this tumor was regarded as a "benign bronchial adenoma." A left total pneumonectomy without drainage was done on March 8, 1939. The surgical specimen was thought to be a spinocellular carcinoma. No metastasis to the lymph nodes was found. The serum pocket became infected and was drained on April 26, 1939. There was evidence of metastasis to the right lung and left femur on May 11, 1939. He died of cerebral metastasis on June 28, 1939.



Fig. 4. Case 4, 6 months after operation. This illustration shows the closure of total esophageal cavity after pneumorectomy by means of thoracoplasty. Not that mediastinum is only moderately shifted to right side.



Fig. 5. Case 5 before operation. This picture shows how large bronchogenic carcinoma may become. It absolutely no symptoms. This tumor is known to have been present for 7 months.

CASE 4. J. H. N. male aged 49 years, had cough with blood streaked sputum which started in November, 1939. A tumor as removed from the left upper lobe bronchus in December, 1939. It was diagnosed as "benign bronchial tumor." There was recurrence of erythema plus pleural pain in June, 1940. X-ray examination showed atelectasis of portion of the upper lobe in November, 1939. The tumor could not be seen by bronchoscopy but secretion as seen coming from the left upper lobe. A left total pneumorectomy without drainage as done on November 7, 1939. There was tumor about centimeters in diameter and about nine-tenths outside of the bronchus. The surgical specimen as regarded as adenocarcinoma of low grade malignancy. There was no evidence of lymph node metastasis. He has been well for years. No evidence of metastasis. The mediastinal shift is marked.

CASE 5. A. G. male aged 5 years, had cough on December 1, 1939. There was blood streaked sputum on December 3, 1939. X-ray films showed atelectasis of the right lower lobe. Bronchoscopy showed tumor obstructing the lower lobe by extending up the bifurcation of the trachea. A right total pneumorectomy as done on January 1, 1940. The microscopic diagnosis as carcinoma of basal cell type of low grade malignancy. The serum pocket became infected and as drained on January 30, 1940. The patient ran fever off and on and lost considerable weight so that he was never in shape for thoracoplasty until October 4, 1940. He still has small draining sinus but is well and has regained his normal weight. There is no evidence of metastasis 3 years after operation.

CASE 6. D. V. male aged 50 years, had cough and blood streaked sputum which were present on August 1, 1939. On October 10 he developed all the signs of pneumonia of the right upper lobe. X-ray films showed

complete consolidation of the right upper lobe in December, 1939. Bronchoscopy showed tumor of the right upper lobe bronchus. It was an adenocarcinoma of grade III malignancy. His temperature rose daily to 102 to 104 degrees F. He was operated upon January 3, 1940. The right upper lobe as hard as gray hepatisation. There were mediastinal metastases. A total right pneumorectomy as done as matter of expediency and 4 or 5 metastatic nodes removed from the mediastinum. The chest was closed with drainage. The patient was greatly improved and was free from fever for the rest of his life. The wound as closed without thoracoplasty. The patient died of metastases on September 1940.

CASE 7. F. G. male aged 40 years, had had lung abscess behind carcinoma for 3 months. His first was by on in September, 1940. He had lost weight from 170 to 135 pounds. His temperature rose to 102 to 104 degrees daily. The tumor as an undifferentiated carcinoma. He was operated upon on October 1940. Gross pus was found in separating the adhesions to get to the mediastinum. Metastases were found in the mediastinal lymph nodes. Because of the gross contamination of the pleura, total left pneumorectomy as done as matter of expediency. The chest as closed with drainage. The patient developed overwhelming infection and died of sepsis on the 8th postoperative day.

CASE 8. C. H. male, aged 55 years, in poor condition as present for 3 years. There was blood streaked sputum in November, 1940, and cough developed since then. There was low grade fever. X-ray film showed atelectasis of part of the right upper lobe. Bronchoscopy showed tumor of the right upper lobe bronchus extending into the right main stem bronchus. A right total pneumorectomy without drainage as done on February 3, 1941. The



Fig 6 Case 16 before operation. This roentgenogram illustrates that a small lesion may produce symptoms early. The lesion shown in the x ray film was due mainly to atelectasis. The tumor obstructing the branch bronchus was only about 5 millimeters in diameter.



Fig 7 Case 17, 1 month after operation. This film illustrates that the mediastinum may not be shifted very much soon after operation. The chest cavity had not yet become completely filled with serum. As the serum clots and is absorbed the mediastinal shift gradually increases.

tumor was an undifferentiated carcinoma of grade III malignancy. No metastasis was seen in the lymph nodes. The serum pocket was drained because of infection on February 14, 1941. The mediastinum came over enough in about 4 months to close the pleural cavity without a thoracoplasty. The patient is now apparently well.

CASE 14 C Y, male, aged 54 years, had recurrent attacks of pneumonia in the right lower chest for about a year. There was mucopurulent expectoration. Bronchoscopy revealed a tumor in the right lower lobe obstructing the bronchus. X ray film showed no aeration in this lobe. The patient was running a low-grade fever. A total pneumonectomy was done without drainage on March 24, 1941, in spite of mediastinal metastasis. The lymph nodes were also removed. Section of the lung showed a tumor about 5 centimeters in diameter. It was spinocellular carcinoma of grade II malignancy. There were large bronchiectatic cavities filled with pus behind the obstruction. The resection of the mediastinal lymph nodes required a visceral pleural patch to close the mediastinal pleura. A thoracotomy was done on April 2, 1941 because of infection. A thoracoplasty was performed on May 7, 1941. The wound is now closed and the patient is apparently well.

CASE 15 R J, male, aged 40 years, in whom at a routine insurance examination a lesion was found by x ray film in the left lung in March, 1941. Since the lesion continued to increase in size for the next 6 months, he was referred to us. Bronchoscopy was negative. The patient had absolutely no symptoms but the x ray film showed the characteristic picture of a bronchogenic carcinoma. A total pneumonectomy was done without drainage on September 24, 1941. The tumor was an adenocarcinoma.

The patient returned to work in his office 6 weeks after operation and has been well since.

CASE 16 W M, male, aged 50 years, had a cough for 2 months with a recent bit of blood streaked sputum. X ray film showed a small area of atelectasis in the left upper lobe. Bronchoscopy revealed spinocellular carcinoma of grade II malignancy. The patient had had no other symptoms and was in his normal physical condition. A total pneumonectomy without drainage was done on October 1, 1941. The carcinoma was found to be only about 4 millimeters in diameter in the upper lobe bronchus. The patient has been perfectly well since operation was performed.

CASE 17 H C, male, aged 62 years, had a 2 year history of suppurative disease in the left lower lobe. Bronchoscopy revealed a stricture of the left lower lobe bronchus with a pure culture of Friedlaender's bacillus. The fifth biopsy revealed spinocellular carcinoma of grade II malignancy. A total pneumonectomy without drainage was done on November 12, 1941. The patient was discharged apparently well after 3 weeks. A low grade fever developed after about a month. Sulfadiazine therapy kept the infection so well under control that drainage was not done until February 2, 1942. A thoracoplasty is yet to be done.

CASE 18 R S, male, aged 63 years, had had a cough for 1 year, bloody sputum and fever for about 6 weeks, and about a 25 pound weight loss in the last 6 months. Diagnosis of carcinoma, squamous cell type, in the right lower lobe was made by x ray film and bronchoscopy. Right pneumonectomy with drainage was done on February 4, 1942. Metastatic carcinoma was found in mediastinal lymph nodes. Convalescence was uneventful. Thoracoplasty is yet to be done.



Fig. 8. Case 8, 8 months after operation. The chest was drained at the time of operation because of infection. The mediastinum is now fixed. The patient is ready for thoracoplasty.

CASE 9. R. C. aged 6 years, had had pain in the right upper chest and shoulder for 8 months. X-ray film showed tumor in the apex of the lung; bronchoscopy was negative. Exploration on February 20, 1933 revealed an adenocarcinoma adherent to parietal pleura. A total pneumonectomy as possible by removing the parietal pleura over the apex of the chest. Enlarged lymph nodes in mediastinum proved to be inflammatory. The chest was drained due to contamination of wound in removing the adherent tumor. The patient has now been free from pain and well for 8 months. A thoracoplasty is yet to be done.

CASE 10. O. J. male aged 64 years, had had bloody sputum for 3 years; pain in the right lower chest for 6 weeks, and 35 pounds loss of weight. X-ray examination showed tumor in the right lower lobe. Bronchoscopy revealed squamous cell type of bronchogenic carcinoma. A right

pneumonectomy was done on February 3, 1933. 3 metastases as found in the mediastinum, but the tumor was freed with difficulty from the diaphragm. No drainage. The convalescence was uneventful. When seen 7 months after operation the patient had gained 35 pounds in weight and appeared well.

#### SUMMARY

The only hope of cure for the patient with bronchogenic carcinoma is surgical removal of the tumor which usually means total pneumonectomy.

2. Total pneumonectomy offers a complete cure for the patient with extensive but unilateral suppurative disease of the lung.

3. The preoperative and postoperative care and certain points in operative technique have been discussed.

4. The mortality in the young patient should be low whether the operation is for carcinoma or for suppurative disease.

5. The mortality will probably remain high in the elderly patient with carcinoma associated with other complicating diseases.

6. Twenty patients are reported upon from total pneumonectomy; has been performed with only 1 death, a mortality of 5.0 per cent.

#### REFERENCES

1. CARPSON, C. On the Technique of Pneumonectomy. In *Mass Sempical Clinic II* of the Balldisburg Hospital. Stockholm: Tryckeri Aktiefelaget. Thirk 1935.
2. FLACK, J. Personal communication.
3. GRAHAM, E. A. and BRUCE, J. J. *J. Am. M. Ass.* 933: 10, 37.
4. HAIGHT, C. *Surg. Gyn. Obst.* 934: 34, 348.
5. LONGWICK, J. J. and JOSEPH, R. *J. Thorac. Surg.* 1930, 3.
6. OVERHOLT, R. H. *J. Thorac. Surg.* 1939-1940, 7-6.
7. RICHMOND, W. T. *Bull. Johns Hopkins Hosp.* 1937, 60: 372.
8. RICHMOND, W. T. *Bull. Johns Hopkins Hosp.* 1938, 53: 350.

# CHRONIC ARTHRITIS

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**A** RTHRITIS is a vague term Denoting inflammation as its basic feature, it has come to include a multitude of other lesions Joint changes in response to allergy, to altered nerve impulse, to metabolic and mechanical imbalance and the aftermath of necrosis and collapse of the articular ends of bones have all been lumped under one name, as years ago the affections of the stomach were made hazy and confused with the now restricted, almost obsolete term, gastritis

## NOMENCLATURE

One hopes that with newer advances the diseases of the joint will be sifted and consigned each to its proper niche in a scientifically valid scheme of classification At the present state of our knowledge, any attempt along these lines would be presumptuous, we do not know the cause of many joint lesions and there are a few whose nature is but vaguely understood Moreover, a classification which would correlate etiological factors with corresponding pathological changes is as yet unthinkable Excluding such well defined entities as tuberculous arthritis, neurogenic arthropathies, gout, and a few others, all one can say of the nebulous mass of chronic joint disturbances is that they are either inflammatory in nature or are the result of wear and tear, of mechanical break-down To be sure, an inflammatory process involving a joint may eventually create mechanical incongruities, and a worn-out joint surface may in time become the nidus of self inflicted irritation and set up an inflammatory focus In other words, inflammatory and degenerative joint lesions may converge into one another, or even coexist

The inflammatory subgroup of chronic arthritis has been qualified as atrophic, proliferative, rheumatoid infectious, progressive, multiple and he-sive, ankylosing or synovial, when occurring in childhood it is referred to as Still's disease The other variety of chronic arthritis has also acquired an array of adjectives hypertrophic, degenerative, traumatic, senile, menopausal, and chondro osseous, it is also called osteoarthritis arthrosis Type II, arthritis deformans ulcerosa,

and Heberdene's nodes No nomenclature has yet been fully agreed upon The English classification designating the two groups as rheumatoid and osteoarthritic makes no commitments as to the as yet unknown cause of chronic arthritis and, although it is neither adequate nor descriptive, it is the least confusing From a pathological standpoint the adjectives *inflammatory* and *degenerative* perhaps come closest to suggesting the primary changes that occur in the two subgroups of chronic nonspecific arthritis

## THE BIOLOGICAL BASIS OF SUBDIVISION

The salient features of the two types can perhaps be brought out by evoking certain basic facts A joint is a connective tissue organ It connects and supports parts and passively permits motion between them In its typical form, a movable, or diarthritic joint consists of a cavity lined by synovial membrane and hyaline cartilage which are respectively supported by fibrous capsule and the articular ends of bones In their evolution from mesoderm these elements follow two patterns one biological, the other morphological Some connective tissue remains relatively undifferentiated, hence highly reactive, in the external stratum of the synovial membrane and in the marrow spaces of the articular ends of bones Specialized, senescent, connective tissue evolves as articular cartilage, trabeculae of bone, the surface layer of the synovial membrane, the ligaments, and the fibrocartilages Structurally the components of the joint are assembled on sound mechanical lines so as to insure a given articulation maximum fulfilment of its function as a unit of support or of passive motion Inflammation primarily affects the reactive elements of the joint—the external stratum of the synovial membrane and the marrow contained in subchondral cancellous spaces, the specialized connective tissues—articular cartilage and trabeculae of bone in particular—are passively displaced by adjacent inflammatory granulations, break down when their elasticity is overcome or degenerate and die in time, the pathological trend is cut off In one instance, the pathological trend is at the start reaction on part of biologically young tissues, in the other the early change is characterized by regression or wearing out of mature, specialized connective tissue elements of joint (Figs 1, 2)

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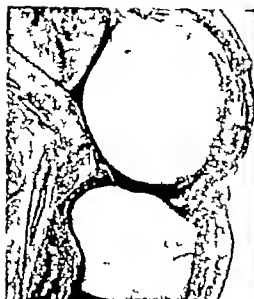


Fig. 1

Figs. 1 and 2. The pattern of evolution of the embryonic joint.

Fig. 2. Embryonic knee. Photomicrograph of the sagittal section of human embryo estimated of 10 weeks intrauterine life. There is distinct morphological change at the stage of future bones already shaped. The slits are rounding the articular ends of femoral bone to form the joint cavity. Not so definitely discernible is the biological differentiation of certain areas as in the bone marrow, the mesodermal tissue remains relatively undifferentiated, hence highly reactive. In others, it evolves as specialized



Fig. 2

connective tissue, the articular cartilage for example. It is proposed that rheumatoid arthritis primarily involves the former and secondarily the latter elements.

Fig. 3. Adult knee. Frontal view of surgically opened knee of young pig. Not the smooth, glistening articular surfaces. The synovial membrane seeds slip over the margins of the articular cartilage leaving its greater central position uncovered. By virtue of its peripheral articular cartilage can react and reproduce itself, the central portion has little or no power of reaction or regeneration.

#### RHEUMATOID ARTHRITIS

The basic feature of rheumatoid arthritis is an inflammatory reaction on the part of the comparatively undifferentiated connective tissues, and granulations thus formed erode and displace specialized elements. The relative vascularity of the external stratum of the synovial membrane and bone marrow favors here the localization of circulating irritants, and in response to the offending agent there ensues hyperemia, edema, cellular infiltration, exudate, and tissue proliferation. The synovial membrane becomes soggy, thickens (synovitis) from its loose areolar spaces, thus it fills seep into the joint cavity (bony ankylosis) when cells pass into the articular cavity or are shed off there results joint exudate. Later finger like processes of proliferated tissue project into the joint cavity (chronic villous synovitis) or they may even break loose and float in the joint fluid (rice bodies, melon seeds). Granulations formed in the external layer of the synovial membrane may extend into the surrounding structures and cause

them to contract (fibrositis, periarthritis adhesions, contract res) or what is perhaps more common, they may break through the barrier of the internal layer of the synovial membrane, creep over the articular cartilage (pannus) erode and destroy it. Usually proliferative activity is going on in the marrow at the same time and the trabeculae of bone are thinned, displaced (atrophy). The cartilage is attacked from below as well and when the opposing cartilages are completely eaten away the granulations contact to form adhesions (fibrous ankylosis) ultimately these connecting strands may ossify and efface the joint completely (bony ankylosis) (Figs. 3 to 10).

Rheumatoid arthritis does not in all instances run through the entire gamut of joint inflammation. The disease may proceed up to one or another phase and then rest itself. If mechanical incongruity has been created—such as eroded articular surfaces, redundant capsule due to overdistention, contractures, subluxations—the joint may in time break down architecturally



Fig 3



Fig 4

Figs 3 to 6 Rheumatoid arthritis active phases of joint inflammation

Fig 3 Hyperemia Arthrograph of the knee of a patient with fulminant rheumatoid arthritis. A few cubic centimeters iodized oil was introduced into the knee and the films were taken every twenty minutes. Already in the first plate opaque material was seen impregnating a large popliteal node and the lymphatics leading to and away from it. Increased vascularity enhances absorption from the joint cavity.

Fig 4 Edema Photograph of the hands showing generalized and localized swelling in and around the proximal interphalangeal and metacarpophalangeal joints

and evolve into the other form of chronic arthritis—joints which are rich in biologically young, vascular, and reactive tissues—joints with extensive synovial membrane and bulbous articular ends which contain a greater amount of marrow tissue—are more likely to be affected by rheumatoid arthritis. Thus rheumatoid arthritis predilects

the knees, the elbows, the metacarpophalangeal and proximal interphalangeal joints. It has been suggested that circulating irritants—bacteria, toxins, allergin, etc.—originating elsewhere in the body as in a distant focus of infection, may give rise to rheumatoid arthritis. However, this causal relationship has not been established beyond the



Fig 5

Fig 5 Cellular infiltration Photomicrograph through section of the synovial membrane. Note the extensive infiltration of cells beneath the synovial surface and the protrusion of the thickened membrane into the articular cavity.

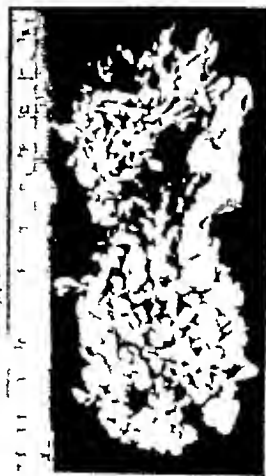


Fig 6

Fig 6 Tissue proliferation Photograph of a segment of surgically removed synovial membrane studded with villi. The latter are finger like processes of thickened tissue on the external stratum of the synovial membrane that invade internal zone and protrude into articular cavity.





Fig. 7



Fig. 8



Fig. 9



Fig. 10

Figs. 7-10. Rheumatoid arthritis, destructive and reparative trends.

Fig. 7. Posture. Photograph of surgically opened knee showing the extension of the synovial membrane over the articular cartilage of the femoral condyles.

Fig. 8. Erosion of articular surface. In this photograph of the knee the articular cartilage is further eroded upon and extra-synovial granulations are continuous with those sprouting from the synovial intussuscept of the cruciate ligaments.

Fig. 9. Adhesions. Photograph of another surgically opened knee. Granulations have contacted and adhered into scars. The jaws of the retractor are hooked to a web band of adhesive blinding the eroded articular surface of femur to the corresponding surface of tibia. This type of joint could eventually evolve into bony ankylosis.

Fig. 10. Creation of mechanical laxation. Photograph of surgically opened knee of man with longstanding rheumatoid arthritis. Granulations resulting from marginal synovial membrane and from the inward meat of the cruciates have deep grooves across the femoral condyles and at their periphery. Clinically the joint was locked and may be revealed it to have passed into osteoarthritic phase. Note the overhanging and protruding spurs.

fact that a certain number of arthritides seem to benefit from eradication of foci of infection. Moreover since some of these patients also suffer from myocardial disease from diminished capillary circulation and develop subcutaneous edema and nodules, it is also inferred that rheumatoid arthritis is perhaps a systemic disease involving not only joints but other derivatives of mesoderm as well (6).

#### OSTEOARTHRITIS

Osteoarthritis occurs most commonly in joints that bear the brunt of daily wear and tear such as the right shoulder in a right handed person. It affects weight bearing joints as the hips, knees and

ankles and, third it predilects joints prior to blood supply as the distal interphalangeal part of the hands. Trauma, acute or chronic is perhaps the main causative factor in osteoarthritis. Instances of acute trauma are found in neglected mechanical injuries, in capsular or ligamentous tears, in subluxations and in intra-articular fractures. Chronic trauma may accrue either within the joint as a result of loose bodies, or may affect the joint indirectly by taxing the lines of stress and strain to which a given area of the articular cartilage is accustomed. Examples of such indirect force causing osteoarthritis are to be found in the weight bearing joints of the obese and in joints near mechanical misalignments flat feet, knock



11 11113 Osteoarthritis causes of degeneration of the articular cartilage

1. 4. 11 and 1. Chronic trauma due to misalignment of articular ends and unwanted friction

Fig. 11. Photograph at the time of arthroscopy of the knee of a man who 18 months previously had received a comminuted fracture of the upper articular end of tibia with displacement of the plateau and throwing of a bony promontory against the medial condyle of the femur. Note the slant of the weight bearing surface from side to side and the impingement of bone jutting up and impinging against the articular surface of the medial condyle of the femur.

Fig. 12 The same after the bony promontory had been chiseled off. Note the two circumscribed areas on the articular surface of the medial condyle of the femur. The cartilage here was soft, pitted and had lost its luster and crested as it were by the abutting bone.

Fig. 13 Chronic trauma excessive pressure. Photograph of the jack knifed knee obtained at autopsy of a man whose weight in life exceeded three hundred pounds. Note the worn-out ragged areas at points of greatest pressure over the articular surface of the femoral condyles. The corresponding surfaces of tibial plateau protected as they are by the semilunar cartilages are comparatively unaffected.

lance, coxa vera, miliumed fractures and particularly trusted epiphyseal growths. Other instances of chronic trauma are also seen in hallux valgus or supraspinatus tendon degeneration when the articular cartilage is forced to rub against rough frayed fibrous or calcareous surface instead of a smooth one. Apart from trauma

age (prolonged triuma), arteriosclerosis, necrosis and collapse of the articular ends of bone, and previous inflammation or infection are also regarded as contributing factors to osteoarthritis (Figs 11 to 13).

In osteoarthritis the mechanical, the specialized elements of the joint are affected primarily

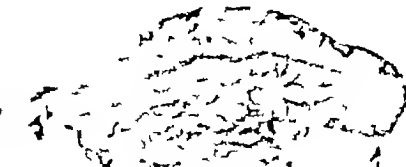
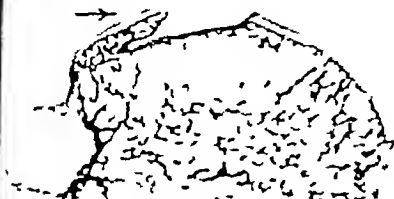


Fig 1

4. The thickness of the articular cartilage. The thickness of the articular surface of the femoral phalanx was measured in the proximal and distal ends for years 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339, 340, 341, 342, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352, 353, 354, 355, 356, 357, 358, 359, 360, 361, 362, 363, 364, 365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394, 395, 396, 397, 398, 399, 400, 401, 402, 403, 404, 405, 406, 407, 408, 409, 410, 411, 412, 413, 414, 415, 416, 417, 418, 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429, 430, 431, 432, 433, 434, 435, 436, 437, 438, 439, 440, 441, 442, 443, 444, 445, 446, 447, 448, 449, 450, 451, 452, 453, 454, 455, 456, 457, 458, 459, 460, 461, 462, 463, 464, 465, 466, 467, 468, 469, 470, 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, 486, 487, 488, 489, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 532, 533, 534, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 560, 561, 562, 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, 576, 577, 578, 579, 580, 581, 582, 583, 584, 585, 586, 587, 588, 589, 590, 591, 592, 593, 594, 595, 596, 597, 598, 599, 600, 601, 602, 603, 604, 605, 606, 607, 608, 609, 610, 611, 612, 613, 614, 615, 616, 617, 618, 619, 620, 621, 622, 623, 624, 625, 626, 627, 628, 629, 630, 631, 632, 633, 634, 635, 636, 637, 638, 639, 640, 641, 642, 643, 644, 645, 646, 647, 648, 649, 650, 651, 652, 653, 654, 655, 656, 657, 658, 659, 660, 661, 662, 663, 664, 665, 666, 667, 668, 669, 670, 671, 672, 673, 674, 675, 676, 677, 678, 679, 680, 681, 682, 683, 684, 685, 686, 687, 688, 689, 690, 691, 692, 693, 694, 695, 696, 697, 698, 699, 700, 701, 702, 703, 704, 705, 706, 707, 708, 709, 710, 711, 712, 713, 714, 715, 716, 717, 718, 719, 720, 721, 722, 723, 724, 725, 726, 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, 744, 745, 746, 747, 748, 749, 750, 751, 752, 753, 754, 755, 756, 757, 758, 759, 760, 761, 762, 763, 764, 765, 766, 767, 768, 769, 770, 771, 772, 773, 774, 775, 776, 777, 778, 779, 780, 781, 782, 783, 784, 785, 786, 787, 788, 789, 790, 791, 792, 793, 794, 795, 796, 797, 798, 799, 800, 801, 802, 803, 804, 805, 806, 807, 808, 809, 810, 811, 812, 813, 814, 815, 816, 817, 818, 819, 820, 821, 822, 823, 824, 825, 826, 827, 828, 829, 830, 831, 832, 833,

[illegible]



Fig. 7



Fig. 8

Fig. 9



Fig. 10



Fig. 11



Fig. 12

Figs. 7 to 11. Surgical measures resorted to in treating rheumatoid arthritis.

Figs. 7 to 11. Skeletal traction to prevent contracture and pressure upon undermined articular surface.

Fig. 7. Photograph of hand in bursoplasty and elastic traction attached to wire passing through the distal phalanx of the middle finger of the left hand.

Fig. 8. X-ray picture of the finger. Elastic traction here is still. The arrow points to the proximal interphalangeal

joint. The distal articular end of the proximal phalanx reveals an area of erosion of the articular surface probably produced by subchondral or marrow granuloma. Motion is encouraged against elastic traction which is maintained for months.

Fig. 9. The same, 3 months later. Elastic traction was removed. Note that the distal articular corner of the proximal phalanx, previously worn eroded, had been in part replaced.

Fig. 10. Photograph of the hand after the bursoplasty had been removed.

Fig. 11. The same. Elastic hand closed showing the articulation of the middle finger.

Fig. 12. Capsulotomy is standard measure for over-closing flexion contracture especially of the knee. It is tamely supplemented with tenotomy and transposition of important nerves. Photograph of the lateral aspect of the knee at the time of posterior capsulotomy and section of biceps femoris tendon. Peroneal nerve is isolated and drawn up with tape. Note the tight tendon of biceps just above it. The blade of the scalpel is inserted into the popliteal space, hugging the posterior aspect of the femoral condyles. It is carried into the knee joint. The biceps tendon is subsequently released and the peroneal nerve is displaced forward to avoid entrapment while the knee is carried into extension.

The highly differentiated, hence less reactive derivatives of the connective tissue—bone and cartilage in particular—bear the brunt of shearing and pressure stresses and break down when their elasticity is overcome or when their nourishment is interfered with as by diminished blood supply which affect the bones, or by scant synovial fluid from which the articular cartilage partly derives its nourishment. At points of greatest friction or pressure the cartilage wears down. It loses its surface gloss, its resilience softens and shreds (chondromalacia) the layer of cartilage nearest the joint as it slowly disappears and the main body of the deeper cartilage splits perpendicularly to the surface (degeneration) the zone of calcifica-

tion underneath cracks, the articular cortex of the bone is laid bare (arthritis ulcerosa) and denuded bone wears smooth by usage (eburnation). Secondly reactive changes take place in the marginal cartilage in the synovial membrane and in the cancellous spaces of the articular ends of bones. In adults, the central pressure-bearing area of the articular cartilage is devoid of perichondrium which elsewhere in the body as in the ribs, has the power of reproducing cartilage. The marginal portion receives a slip from the synovial membrane and can repair itself in response to unwearied stress put upon it by incongruous articular surfaces, the marginal cartilage thickens (hypertrophy) swollen areas may bulge out on



Fig 23



Fig 24

Figs 23 to 31 Synovectomy is another standard surgical procedure and is especially beneficial in persistent hydrops and in chronic villous synovitis

Figs. 23 and 24 Synovectomy, the operation  
Fig 23 Photograph of the surgically opened right knee of a man with rheumatoid arthritis who, 9 years previously, had a synovectomy performed on his left knee with a fair

restoration of function and no recurrence of effusion Note that the synovial membrane is thrown into numerous folds and villi and its secreting surface is thus greatly expanded Also observe that the inflamed membrane has grown across the articular cartilage and partly eroded it

Fig 24 Photograph of the knee immediately after dissection of turgid thickened synovial membrane



Fig 25



Fig 26



Fig 27



Fig 28

Figs 25 to 28 Synovectomy, postoperative mobilization of the joint This is started 3 days to 2 weeks after synovectomy, depending upon the degree of pain and the patient's willingness to co-operate

Fig 25 Photograph of an improvised three way traction outfit A 5 to 10 pound weight is applied to an ankle made of felt or canvas The patient forces the knee into flexion by means of a rope going over pulleys to a sling under the

knee As the perpendicular pull is released another 5 pound weight attached to a rope passing through a hole in the mattress forces the knee into hyperextension

Fig 26 Close up photograph of the three way traction outfit.

Fig 27 Photograph of the ankle made of canvas instead of the original felt.

Fig 28 Photograph of the two way knee sling



Fig. 29



Fig. 30



Fig. 31



Fig. 32



Fig. 33

Figs. 29 to 31. Synovectomy functional results.

Fig. 29. Knees of woman who underwent bilateral synovectomy the left knee 3 years ago the right knee 1 year ago.

Fig. 30. Photograph showing the degree of flexion obtained 1 year after operation of the right knee.

Fig. 31. Photograph demonstrating the degree of flexion obtained 3 years after synovectomy of the left knee.

Figs. 32 and 33. Removal of incongruities. This operation is not recommended in most bony joints. However, if both hips and knees are interlocked or ankylosed it becomes expedient to mobilize one knee and opposit hip.

Fig. 32. Surgically opened knee shows in Figure 30.

Fig. 33. Same immediately after smoothing out crater like mechanical incongruity chiseling off osteophytes, and marginal synovectomy. Patella as reduced in size and reshaped. Some operators remove it completely.

Figs. 34 to 40. See

Figs. 34 to 37. Osteotomy deformities in rheumatism it is resorted to with the points and putting the sound articular surfaces under

Fig. 34. X-ray picture of iliofemoral acetabulum and pelvis was similarly affected.

Fig. 35. The same immediately post were introduced, one at the hip just beneath the greater trochanteric osteotomy was performed. The plates the fragments into desired position and one another outside of the body and/or short open cast. Note that the femoral



Fig 34



Fig 35



Fig 36

levered deep into the acetabulum and is somewhat rotated anteriorly. The lower fragment is displaced medially.

Fig 36 The same 2 months later. Union has already taken place and the head of the femur is deep in acetabulum.

Fig 37 Composite photograph of the patient a year later showing the stability of the left hip and its range of motion. This hip had ceased to hurt patient, the right hip, as yet untouched for purposes of control, continued to cause pain.

Figs. 38 to 40 Arthrodesis

Fig 38 Photograph of the bowed left knee of a man of 58 who some 30 years ago injured this knee which became markedly swollen. The swelling recurred for years after and at the time of examination the capsule of the joint was so lax that the knee wobbled from side to side as in a Charcot joint. Motion, however, was painful and there was no anteroposterior instability indicating intact cruciates.

Fig 39 Photograph of the knee at arthrotomy. Note the deep ulcer over the articular surface of the medial femoral condyle where most of the weight was borne.

Fig 40 Photograph showing the stability of the knee 6 months after fusion.



Fig 37



Fig 38

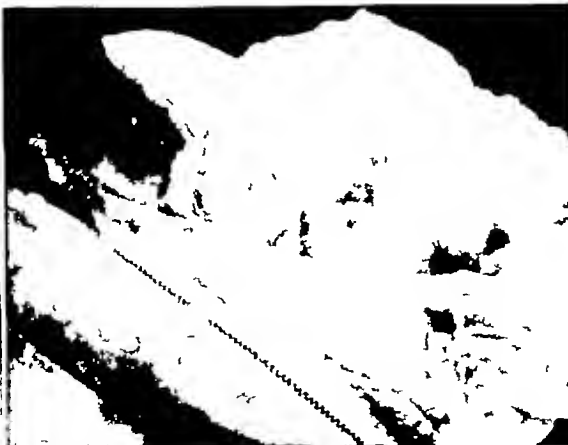


Fig 39



Fig 40

## COMPARISON OF RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

	Rheumatoid arthritis	Osteoarthritis
Primary source of origin	Systemic, proliferative in location, inflammatory etc.	Periarticular, degenerative, traumatic, arthralgia, etc.
Duration and evolution	Under 50 years, pain, swelling, loss of motion	Over 50 years, recurrent pain, swelling, loss of motion
Systemic reactions	Fever, leucocytosis, increased sedimentation rate may be present	Absent
Joint involvement	Those such as proximal carpal, distal interphalangeal, etc. are common. Proximal interphalangeal and distal interphalangeal are less common. The proximal interphalangeal is common.	Weight bearing, locomotor joints and those joints of the extremities, like the distal interphalangeal.
Symptoms	Pain and stiffness, morning joints involved	Pain and stiffness, morning joints involved
Pathology	A. Primary inflammation of synovial membrane (thickening of the joint) and of the articular surface. B. Secondary: Inflammation of the articular surface and of the articular surface.	1) Primary: Wearing down of the articular surface of the joint and of the articular surface and of the articular surface. 2) Secondary: Reactive process at the margins in the form of spurs.
X-ray	Enlargement of soft part, disappearance of cartilage space, erosion of the articular surface, subluxation, contracture, and ankylosis.	Wearing down of articular surface of the joint, disappearance of the space in the joint, erosion of the articular surface, subluxation, contracture, and ankylosis.
Response to treatment	Responds to systemic disease and treatment of the patient as a whole, resulting in measures that would improve the health, prevent deformity.	Direct attention to the joint itself, including measures to prevent further damage, but not to the systemic disease of the body.
Surgery	Not of primary importance, but of secondary importance in the treatment of the patient as a whole, resulting in measures that would improve the health, prevent deformity.	Indicated as a primary measure of treatment of the patient as a whole, resulting in measures that would improve the health, prevent deformity.

the surface (epiphyseal echondroses) or they may project peripherally (marginal echondroses). Surface swellings further enhance the existing incongruity and marginal growth within the bearing area of the joint. These nodules may become vascularized and receive a bone core (chondro-osteophyte) they may be completely ossified (osteophytes) they may detach and break free in the joint cavity (osteoarthralgous loose bodies). Marginal spurs encroach upon the synovial membrane and irritate it toward inflammatory reactivity and analogous proliferation is set up in the

cancellous spaces of the bone which replace the trabeculae and create cavities containing fibrous tissue or fatty marrow (cystic degeneration). The opposed articular surfaces may interlock in osteoarthritis, but true ankylosis does not occur, a nodular thickening of the marginal cartilage prevents the central ulcerated areas from contacting (Figs. 14 to 16).

## CLINICAL DIFFERENTIATION OF THE TYPES

Rheumatoid arthritis is more generalized and affects many joints osteoarthritis is more or less confined. The symptoms of pain and stiffness are far more severe in rheumatoid arthritis and are more frequent. The joint manifestation associated with myocardial heart disease, subcutaneous nodules, vasculitis, proctitis, anemia, etc. osteoarthritis may accompany menopause, obesity, arteriosclerosis, congestive heart disease, chronic bronchitis and bronchiectasis and, lastly, mechanical misalignments of the body. Ankylosis of the joints in rheumatoid arthritis may, in the earlier stages, reveal fusiform swelling of the soft parts, somewhat later disappearance of the joint space, and erosion of marginal articular cortex and porotic bone. In late stages one may see evidence of contractural deformities, of subluxations and ankylosis. Films in osteoarthritis would reveal disappearance of the joint space, a pressure point, sclerosis of the bone below cyst like formations in the articular ends, marginal spurs, and osteoarthralgous loose bodies in the joint.

## THE TREATMENT OF RHEUMATOID ARTHRITIS

In treating arthritis it is safe to regard the rheumatoid variety as a generalized, systemic disease and treat the patient as a whole in the initial stages. It is well to prescribe complete physical rest splinting the joints in optimum position of function should ankylosis intervene. The latter could at times be obtained by making the splints removable so as to permit periods of guarded exercise. If better still, one may resort to traction and countertraction instead of fixed splintage. All measures which may contribute to the general well being of the patient should be undertaken: high caloric high vitamin diet, tonics, cathartics, analgesics, sedatives, spas, etc. Foci of infection are eliminated to give the patient the benefit of the doubt, and recourse may be taken to gold injections and vaccines as there is at least a relatively rational basis for resorting to parenteral therapy in generalized disease like rheumatoid arthritis, which might be cured or aggravated by infections and which is hopeless at times. Thus during the earlier stages of rheumatoid

toid arthritis measures resorted to are mainly medical and systemic. The surgeon veers his attention toward the local manifestations of the disease as aspirating overdilated joints, splinting painful ones and applying various forms of traction and countertraction to prevent deformities.

Apart from exercise, traction, and splintage, numerous local measures are undertaken in rheumatoid arthritis. Joint lavage with physiological salt solution is occasionally carried on to remove thick flocculent exudate from the articular cavity, and the articular ends of bones are drilled by some with the purpose of releasing pent-up granulations from the cancellous spaces (forage). Massage, heat therapy, histamine, and mecholyl iontophoresis are resorted to with the idea of improving local circulation. Massage and manipulation is not begun until the sedimentation rate has become normal and the joint inflammation has subsided. At times it becomes expedient to inflate the joint with air, oxygen, saline, or iodized oil, and then manipulate it. Injection of such material purports toward breaking or slackening adhesions. Manipulation should not be forceful, it is safer to use less force and repeat the procedure. A joint requiring great force had better be operated upon so as to sever tough adhesions surgically—either within or around the joint capsule. In smaller joints it might be wiser to enhance intra articular adhesions in order to eliminate painful motion. This is done by injections of sclerosing solutions (quinine urea hydrochloride) and immobilizing the joint for a long time. Capsulectomy, osteotomy, or tenotomy aim at correcting resistant deformities. The same end may also be attained by wedging the cast and correcting the deformity by a well placed turnbuckle. Deformities may likewise be corrected by skin or skeletal traction. Synovectomy is sometimes resorted to when the inflammation has left an extensive ever-secreting surface (hydrops, chronic villous synovitis). As to the comparative value of arthrodesis and arthroplasty, it can in general be stated that one must aim toward procuring a mobile joint in the upper extremity and a stable, even though stiff, one in the lower. Therefore arthroplasty, especially of an old ankylosed elbow, is at times commendable. A stiff painless knee or ankle, when in good position, had better be left alone. When

both hips and knees are ankylosed one may compromise at mobilizing the hip on one side and the knee on the other, leaving a painless fused hip and knee. In rare instances the bones are shortened to release contracted tendons. Removal of one or both rows of carpal bones would accomplish the same (Figs 17 to 33).

#### THE TREATMENT OF OSTEOARTHRITIS

The treatment of osteoarthritis is mainly local. Obesity when present is reduced by regulated doses of thyroid and diet, postural defects indirectly affecting the joint are corrected. Painful joints are supported by fixed or ambulatory splints. Heat, massage, and analgesics are prescribed to alleviate pain. Arthrotomy is at times performed for removing osteocartilaginous loose bodies, occasionally painful osteophytes are chiseled off, irregularities of articular surfaces smoothed (cheilotomy, debridement, reconstruction, erosion). In the hip, of late, vitallium arthroplasty has come into vogue, at times, again in malum coxae senilis, osteotomy is performed so as to shift the weight-bearing lines and proffer an undamaged articular surface under the lines of stress and strain. Arthrodesis is performed to eliminate crumbled weight-bearing joints (Figs 34 to 40).

#### SUMMARY

The accompanying table attempts to recapitulate and contrast the basic features of the two great forms of chronic nonspecific arthritis.

#### REFERENCES

1. ALLISON, NATHANIEL, and GHORMLEY, R. K. *Diagnosis of Diseases*. New York: William Wood & Co. 1931.
2. CECIL, RUSSELL L. *Oxford Monographs on Diagnosis and Treatment*. Vol. VI. New York: Oxford University Press, 1936.
3. FLY, LEONARD W. *Inflammation in Bones and Joints*. P. 16. Philadelphia: J. B. Lippincott Co., 1923.
4. FISHER, A. G. TIMBRIELL. *Chronic (Non Tuberculous) Arthritis*. Pp. 7-35. London: H. K. Lewis & Co., Ltd. 1929.
5. HENCH, P. S. *Acute and Chronic Arthritis*. *Orthopedic Surgery*. New York: Thomas Nelson and Son, 1938.
6. KELIKIAN, H. *Surg. Gyn. Obst.* 1940, 71: 416-436.
7. MACNUSON, P. B. *Surg. Obst. Gyn.* 1941, 73: 1-9.
8. NICHOLS and RICHARDSON. *J. Med. Res.* 1900, 16: 140.
9. OSGOOD, R. B. *J. Bone Surg.* 1926, 8: 1.
10. WILSON, P. D. *J. Bone Surg.* 1929, 11: 40.



# OSTEOCHONDROMAS ARISING FROM THE BASE OF THE SKULL

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**I**NTRACRANIAL tumors of cartilaginous structure are among the most unusual types of neoplasm encountered by the neurologist or surgeon. Such lesions may arise from the meninges or from the bones of the skull. The meningeal chondrosarcomas appear to be an unusual variant of the common meningioma. Approximately 30 of such cases have been hitherto reported, and a good review of the literature pertaining to them is given by Chorobski, J. Krymki, and Ferens.

The osteochondromas arising from the base of the skull exhibit a characteristic anatomical and clinical picture, the description of which is the purpose of this study. In view of the rare occurrence of the basal osteochondroma as many observations as possible were utilized. The author was fortunate enough to be able to review a composite material of 7 examples: 5 cases were seen in the University of Michigan Hospital (3 of these were personal observations) and 2 were taken from Dr. Harvey Cushing's series of intracranial tumors, having been made available to me through the kindness of Dr. Louise Elsenhardt, in charge of the Brain Tumor Registry in New Haven.

The illustrative case histories to follow will be divided into two groups (1) primarily intracranial osteochondromas, arising from the sphenoid bone (5 cases) and (2) primarily extracranial osteochondroma of the ethmoidal or sphenoidal region with secondary intracranial extension (2 cases).

## REPORT OF CASES

### *Primarily intracranial osteochondromas arising from the sphenoid bone*

**CASE.** Sanford D. No 47732, U of Mich. Hosp., male, aged 34 years, as referred by Dr. F. Barbauer of Flint. Patient presented the clinical syndrome of right-sided parietal lesion of several years' duration. There was roentgenographic evidence of parietal and retro-

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Variety of cases of chondroma of the ethmoid and sphenoid areas are recorded in the osteological literature (H. Key) but only those with neurological symptoms (intracranial extension) will be considered here.

ocular calcification. Osteoplastic craniotomy was performed, with apparently complete removal of an extral osteochondroma. Patient recovered but with residual neurologic signs.

For 7 years prior to admission, the patient gained weight rapidly until he reached the weight of 270 pounds. At the same time he noted increasing thirst and polyuria. Two years before admission, vision of the right eye began to fail. This progressed gradually and later he noted weakness also on the left. For the 6 months prior to admission he had suffered from paroxysmal right frontal-occipital headaches and retro-orbital pain, occasionally accompanied by vomiting, and had experienced dizziness and tremors. Recently he had become incontinent and complained of numbness of the right half of the face.

Examination revealed the following: Patient was very obese man, weighing 270 pounds, with dorsal kyphosis and sparse beard otherwise there were no constitutional changes. He showed no gross mental change except for slight euphoria and indifference. There was mild right temporal and supraorbital tenderness. Visual acuity was 6/60 on the right and 6/45 on the left. The right optic disc showed slight temporal pallor. A partial homonymous hemianopsia to the left and bilateral paracentral scotomata were present. The mydriatic right pupil did not react to light and on accommodation, but the left pupil was normal. There were considerable paresthesia of the right superior rectus, and slight paresthesia of the inferior oblique and inferior rectus. Although the corneal reflexes were normal and equal, sensation of the right cornea was slightly diminished and cutaneous hypesthesia existed over the left trigeminal division on the right. The patient showed no nasal, left lower facial weakness or right numbness of the left arm. Deep reflexes were slightly hyperactive on the left, with pathologic Hoffman reflex. The left abdominal reflexes were diminished.

Roentgenograms of the skull revealed slight erosion of the dorsum sellae. There was, however, no distinct intracranial calcification in the right parietal, sphenoidal and retro-orbital areas. It extended from the anterior claud to the petrous ridge, covering the floor of the right middle fossa (Fig. 1).

Diagnosis: Right parietal and retro-orbital presumably calcified meningioma or osteochondroma. A craniopharyngioma was also considered as a highly diagnostic possibility.

Operation: As performed March 2, 1921, by Drs. C. F. List and M. M. Peet. Local anesthesia, supplemented by intra-cerebral sodium pentothal, as used. A right frontotemporal osteoplastic craniotomy as performed followed by subtemporal decompression. After the dura opened, the brain appeared under no increased tension. Inspection of the ethmoidal region showed the right optic nerve and carotid artery to be displaced forward, but no tumor was visible. An exploratory needle introduced into the second temporal convolution toward the base met first resistance at depth of 3 centimeters. Through the anterior two-thirds of the right temporal lobe, an unusual nodular tumor the size of large plum, was seen to arise extracranially from the base of the skull, below and to

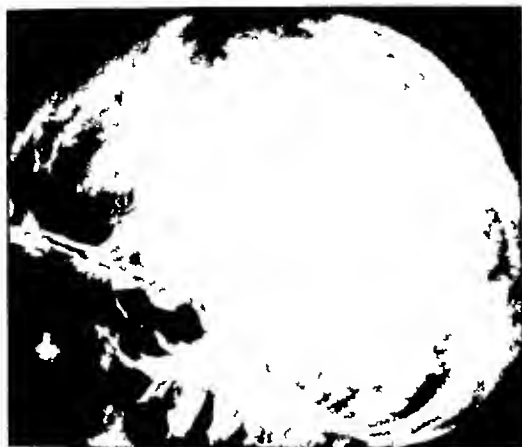


Fig 1 Roentgenograms<sup>1</sup> of intracranial basilar osteochondromas Calcified parasellar tumors in lateral projection a, left, Case 1, b, Case 4

occupy the entire parasellar and retrosellar area, where it had penetrated the dura (Fig 3). The grayish white tumor was firm and gritty in parts due to calcification. It had the typical appearance of an osteochondroma. At first, the main bulk of the tumor was removed piecemeal, and then its attachment along the cavernous sinus and posterior clinoid process was exposed by splitting the basilar temporal dura. Considerable hemorrhage from the superior petrosal sinus and veins surrounding the gasserian ganglion was controlled by electrocoagulation. After the dura was split over the clivus the tumor was seen to extend both extradurally and intradurally in front of the pons, but the arachnoid (basilar pontine cistern) was intact. The right 3d, 5th, and 6th nerves were exposed. All visible tumor tissue was removed.

**Histologic report.** Cartilaginous tissue with large areas of degeneration, calcification, and bone formation. Diagnosis: Osteochondroma (Fig 5, a).

Immediately after operation the patient showed total paralysis of the right 3d, 4th, 6th, and 7th nerves, and increased involvement of the 5th nerve. Furthermore, there was marked loss of vision in the right eye, moderate left hemiparesis and homonymous hemianopsia. However, on patient's discharge from the hospital, 17 days after operation, the left hemiparesis had cleared up completely.

When the patient was last seen, a year and 10 months after operation, he had no complaints except for two generalized convulsive attacks. He stated that the polyuria and polydipsia had disappeared. Examination revealed the area of decompression to be sunken in. There was still paralysis of the right 3d and 4th nerves, and paresis of the 6th and 7th nerves, but the 5th nerve had recovered completely. Vision was normal, but bilateral mild primary optic atrophy and a slight left hemianopic field defect was demonstrable. Check up roentgenograms of the skull showed no evidence of recurrence, viz., absence of calcifications and unchanged position of the silver clips in comparison to the first postoperative films.

**CASE 2.** Celena M. LeB., Peter Bent Brigham Hospital, Surg., Nos. 21293 and 40491, female, aged 26 years, was referred by Dr. M. V. Tyrode, Boston. Right parasellar syndrome had been present for 3 years. There was roentgenographic evidence of right parasellar calcification. An

osteoplastic craniotomy with subtotal removal of parasellar osteochondroma was done. Patient was followed up for 17 years after operation, eventually she showed signs of recurrence of tumor with extension into the right cerebellopontine angle.

Three years prior to admission the patient noted numbness of the right side of the face associated with swelling of the right eyelid. This gradually receded, except for residual numbness of the right half of the forehead. With the onset of numbness, the patient experienced diplopia, especially on downward gaze. A few months later, she complained of right supraorbital headaches which were occasionally associated with vomiting. Two years before admission the right pupil became dilated and vision of the right eye slowly declined. Menstruation remained normal.

Examination revealed the following: Patient was of normal constitutional type and free from gross mental disturbances. The right temporal region was tender to percussion. Vision was 20/20 in left eye, 20/30 in right eye. There was slight right optic atrophy with mild concentric contraction of the right visual field. The dilated right pupil hardly reacted to light and on accommodation. There was incomplete paralysis of the right 3d nerve, namely paralysis of the inferior rectus, moderate paresis of the superior rectus and inferior oblique, and slight weakness of the medial rectus. The right 4th nerve was totally paralyzed, the right 6th nerve paretic. There was hypesthesia in the ophthalmic division of the right 5th nerve, with depression of the corneal reflex, mild hypesthesia was present also in the second trigeminal division. The deep reflexes of the left upper extremity were increased and the left abdominal reflexes were diminished.

Roentgenogram of the skull showed that the right anterior clinoid process was slightly eroded. There was a dense right parasellar calcification of cauliflower appearance extending from the lesser sphenoidal wing almost to the midline and outward to the middle of the right temporal fossa.

**Diagnosis.** Calcified right parasellar tumor, presumably a meningioma arising from the inner portion of the right sphenoidal wing. An osteochondroma was also considered.

Operation was performed on May 12, 1924 under ether anesthesia by Dr. Harvey Cushing. A right sided low osteoplastic flap was turned and a subtemporal decompression added. When the dura was opened, the brain was

<sup>1</sup>Roentgenograms were slightly retouched before reproduction.



Fig. 1. Calcified parasellar tumor extending into the sella, occipital projection.



Fig. 2. Calcified parasellar tumor extending into the cerebellopontine angle, Case A, left lateral projection.

found to be of normal appearance and under no increased pressure. Elevation of the temporal lobe, however, revealed smooth, rounded, extradural tumor arising from the posterior medial part of the right middle fossa. When the overlying dura was incised the tumor was found to have the appearance of soft chondroma containing yellowish calcified areas. 5 grams of the growth, including its anterior pole, was removed piecemeal. Hemorrhage from the rebed of the tumor was controlled by muscle packs.

**Histologic report.** The tumor was calcifying mesenchondroma.

After operation, there was complete right ophthalmoplegia, but the trigeminal symptoms cleared up. Check-up roentgenograms showed few remaining calcifications in the right middle fossa. The ophthalmoplegia began to improve 3 months after operation, and re-examination 3 years later showed only residual paralysis of the 6th nerve and palsy of the right pupil. After 3 years of postoperative observation, however, signs of recurrence became evident. She complained of right front occipital headaches and dizziness. She also suffered from attacks of general collapse associated with facial flushing and peculiar epigastric sensations, usually after breakfast. On one occasion she apparently had an epileptic seizure.

When she finally began to complain of stiffness of the neck and untidiness of the hair, she was readmitted to the hospital (on February 5, 1935, almost 8 years after her first admission). At that time marked decrease of vision of the right eye and bilateral mild secondary optic atrophy were noted. The right ophthalmoplegia and the lesion of the first and second trigeminal branches had recurred. In addition there were slight cerebellar and cerebellar signs on the right. Roentgenographic examination showed considerable increase of the calcified mass, especially in the retrosellar area, its extension into the right cerebellopontine angle (Figs. 3a and b). Patient was discharged after operation.

She was last seen on May 7, 1941—6 years after operation and 20 years after onset of her disease. At that time the clinical picture was almost unchanged, but roentgenograms showed increase of subtle oval calcification. Case 1. Hek. L. Peter Bent Singson Hospital, Surg. N. Y. female aged 20 years, as referred by Dr. Charles F. Heger, New York, New York. Patient gave

6-year history of right-sided calcifying parasellar chondroma. Removal of neoplasia elsewhere had been done 3 years before admission. A second operation with removal of recurrent tumor was carried out but there was gradual spread of the lesion to the chiasmatic region and cerebellopontine angle. Death occurred 3 months after second operation. No autopsy was performed.

Six years prior to admission, the patient complained of blurred vision on the right. A few months later she began to suffer from sharp right supraorbital pain and generalized headache which were sometimes accompanied by nausea and vomiting. Four years before admission her eye noticed pain in the right half of the face followed by numbness, first of the forehead, later of the right cheek. Shortly thereafter right ptosis and an inward squint developed. Two years before entrance, she became almost blind in the right eye. At that time (right) Dr. Heger removed chondroma of the right middle fossa by means of subtemporal decompression. After temporary improvement of the ocular symptoms, there was evidence of recurrence, vision again failed on the right, double the right eye began to protrude. She experienced similar seizures, lasting for a few seconds. An underrated frightening sensation rushed through her body lasting for 10 and sometimes 20 seconds. She had complained of occasional tremors and had been amenorrheic for the past year (result of ray therapy).

Examination revealed the following essential findings. The apprehension, highly stressed patient showed an operation scar in the right temporal region with bone defect (decompression). Anesthesia over the area described showed isolated brain lesion as reduced to light perception on the right but as normal on the left. The right visual field could not be taken; the left one showed slight constriction. There was right primary optic atrophy, the left optic disc normal. The enlarged right pupil reacted only slightly to light and on accommodation. There was total paralysis of the right 3rd nerve and palsy of the right 4th and 6th nerves including right ptosis. The first and second divisions of the right trigeminal nerve were anesthetic; the third division was hypesthetic. There was corneal anesthesia and palsy of the innervation muscles on the right.

Roentgenogram of the skull showed right parasellar erosion with scattered areas of calcification in the right parasellar and temporal regions.

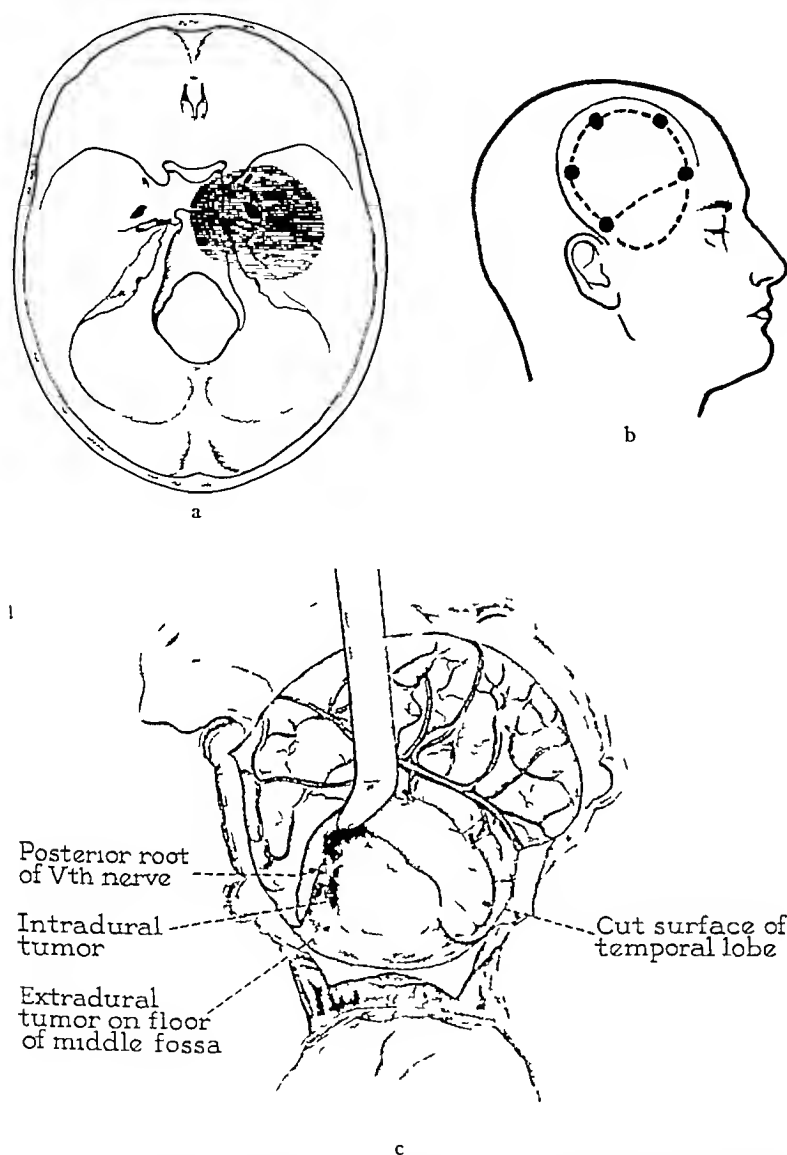


Fig 3 Basilar osteochondroma, arising from the right parasellar region Case 1  
 a, Diagram showing the tumor projected on the base of the skull Attachment of  
 tumor is cross-hatched b Drawing to show operative incision and osteoplastic flap  
 c, Tumor exposed at operation, after partial resection of the right temporal lobe

**Diagnosis** Recurrent calcifying chondroma in the right parasellar region

**Operation** was performed on June 30, 1928, under local anesthesia, by Dr H. Cushing. A right temporal osteoplastic flap was turned and the dura was opened. After incision of the second temporal convolution, a hard nodular chondroma was exposed, arising from the base of the skull. The tumor was firmly attached to the tentorium and floor of the middle fossa. It extended forward beyond the sphenoidal wing which was eroded, and posteriorly to the

incisura tentorii. The neoplasm was removed by piecemeal enucleation, and weighed 28.5 grams. Considerable hemorrhage from the base, presumably from an enlarged middle meningeal artery, was controlled by implants of muscle.

**Histologic reports** The fresh specimen examined by supravital technique, showed the picture of a chondroma. This was confirmed by stained preparations which revealed irregular islands of cartilaginous cells surrounded by a collagenous or mucinous matrix. The neoplasm was considered as a nonencapsulated chondroma likely to recur.



FIG. 4. Roentgenograms of previously extracranial osteochondroma, with intracranial extension. a, Unfractured view of the sphenoid and paranasal sinuses destroying the base of the skull. Case 6. Bender projection. b and c, Frontotransverse, osteochondroma/sphenoid. Case 7. b, Posteroanterior projection. c, lateral projection.



The patient showed total right ophthalmoplegia after operation, but her headaches were relieved for 6 months. They then recurred and there was rapid progression of abnormal neurologic signs. When the patient was re-examined a year after operation, the subtemporal decompression was being. The right eye was blind and showed neuropathic keratitis. There were optic atrophy and temporal hemianopsia on the left. The right 3d, 4th, 5th, and 6th nerves were completely paralyzed and the 7th and 8th nerves paralytic. Check-up roentgenograms showed increase of paranasal erosion with partial destruction of the right lesser sphenoidal wing and petrous apex. The calcifications also had increased and the silver clips were displaced in comparison to previous films. Evidently the tumor had recurred and extended forward toward the chiasm as well as posteriorly into the right cerebellopontine angle. One month later the patient died as reported. N. autopsy was obtained.

The entire known duration of the disease in this patient case was 7 years.

CASE 4. Bertha S. U. of Michigan Hospital, No. 469783, female, aged 50 years, as referred by Dr. W. D. Tomaley, St. Joseph, Michigan.

Patient suffered an acute onset of paresthesia of the right 3d and 4th cranial nerves without neurovascular changes of the skull. Intracranial aneurysm of the internal carotid artery was suspected and the right common carotid artery was ligated. Twenty months after onset, typical right cavernous sinus syndrome, cavernous bone destruction and calcifications in the right paranasal region had developed. Osteoplastic craniotomy was performed and subtotal removal of an extracranial osteochondroma was accomplished with symptomatic relief.

Since adolescence, the patient had suffered from right-sided menstrual irregularities. Four weeks prior to her first hospital visit, on July 8, 1930, she had had severe pain, and then the right eye, occurring especially at night. Three days after onset of pain, the right upper eyelid drooped and became puffy; diplopia developed, and most of the right eye began to fall. Examination revealed marked paresthesia of right 3d and 4th cranial nerves without other neurologic manifestations. Roentgenograms of the skull were normal.

The patient, as seen again 6 months later, has the complained of increased pain in the right frontal and nasal areas. In addition to the paresthesia of 3d and 4th cranial

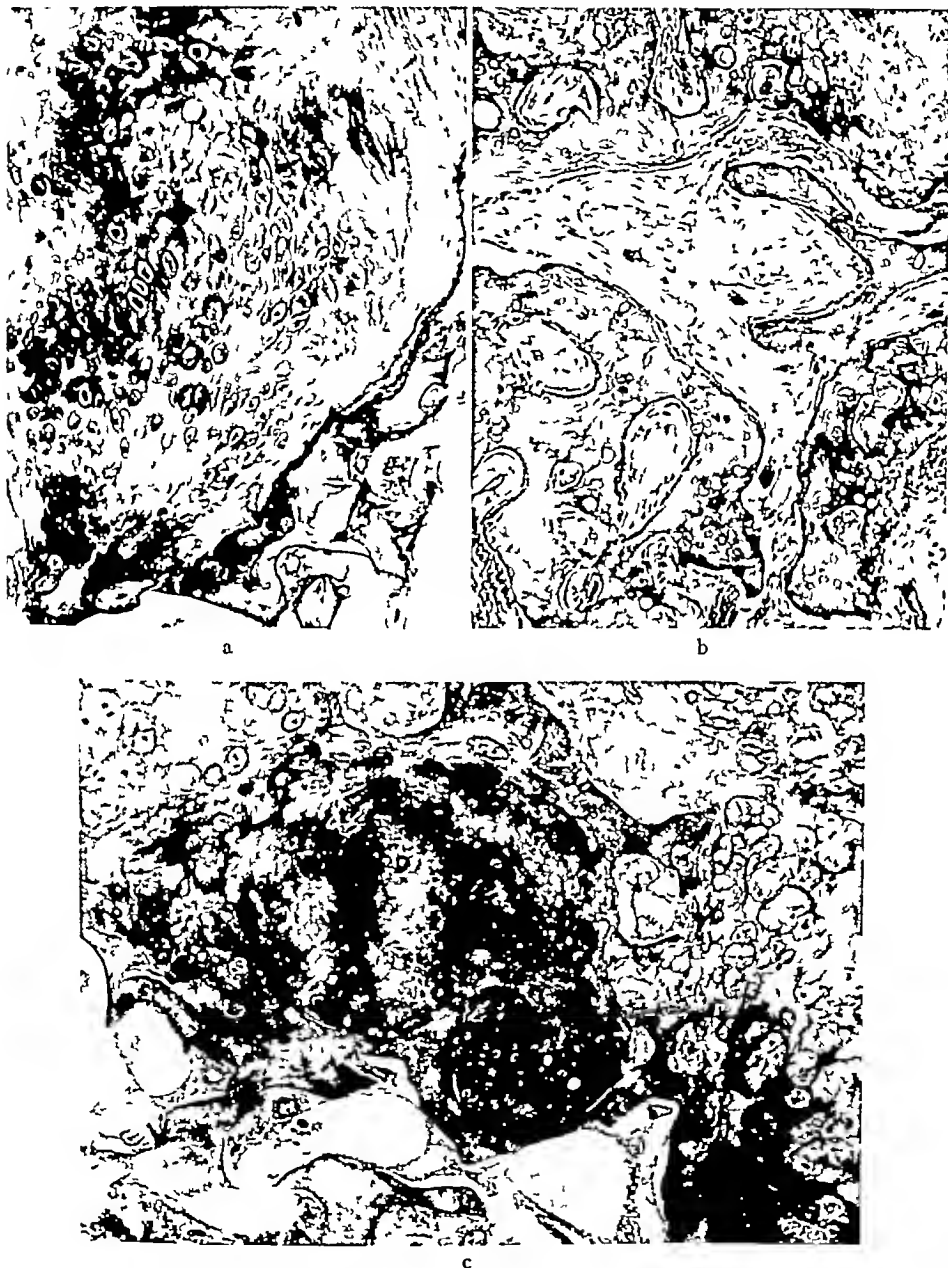


Fig 5 Histologic sections of osteochondromas a Case 1, osteochondroma, b, Case 4, osteochondromyxosarcoma, c, Case 6, osteochondroma

paralysis of the right 6th nerve and supraorbital hyperesthesia had developed. Two months later, the patient again returned because of the almost continuous and severe pain in the right frontal, orbital temporal, and malar regions. Pain often was associated with nausea, vomiting and photophobia. Objective clinical findings were unchanged.

A tentative diagnosis of intracranial aneurysm of the right internal carotid artery was made. Arteriography of the right common carotid artery failed to demonstrate the internal carotid, but showed filling only of the external carotid. The roentgenograms also revealed a small flake of calcium in the right parasellar area which was then

interpreted as being in the wall of the supposed aneurysm. Ligation of the common carotid artery performed, but afforded no relief.

The patient was not seen until 3 years later (March 3, 1914). She then stated that after temporary improvement, the pain in the right side of her head had become unbearable. One month prior to this last, left, thrombosis developed over the right side of the forehead and cheek, and vision of the right eye had become very poor.

Examination revealed the following: Patient was suffering from severe pain in the right frontal, temporal, and malar areas, and complained of nausea and photophobia. The right temporal and supraorbital regions were tender to percussion. The right upper eyelid showed ptosis and slight edema. Mild exophthalmos, as noted on the right. Signs of involvement of cranial nerves were confined to the right side as follows: Hypoesthesia marked reduction of visual acuity (1/60 right eye) concentric constriction of visual field. Enlarged blind spot and slight pallor of optic disc; total paralysis of the 3d, 4th, and 6th cranial nerves. The right corneal reflex was abolished and all forms of sensation were markedly diminished in the area supplied by the first trigeminal division and moderately impaired in that of the second division. There was also slight atrophy and weakness of the masticatory muscles. On the left side, the deep reflexes of the extremities were slightly increased and positive Babinski sign was elicited.

Röntgenograms of the skull revealed extensive destruction of the sella turcica, sphenoidal sinuses, basilar bone and medial parts of the floor of the right middle lobe. There were dense calcifications in the left parasellar region extending from the inner portion of the right middle lobe slightly beyond the maxilla (Fig. 1b).

Diagnosis: The previous diagnosis of carotid aneurysm as now considered untenable and right parasellar osteochondromatosis as suspected.

Operation as performed on March 30, 1914, under ethyl anesthesia, by Dr. C. F. East. A right-sided fronto-temporal osteoplastic flap as turned and combined with subtemporal decompression. After the dura was opened, the brain showed wide subarachnoid channels and as under no increased tension. Inspection of the chiasmatic region revealed the right optic nerve to be displaced forward.

After resection of the lower third of the anterior part of the nasal lobe an extradural tumor as exposed at the medial part of the right middle lobe. The lesion

the size of plum and felt soft, almost fluctuant. Aspiration yielded brownish gelatinous tumor tissue. Thereupon the bulging dura as incised, thus exposing the smooth, vascular surface of the tumor over which the first and second trigeminal branches were considerably stretched and displaced. These nerves were resected. The tumor removed piecemeal and by suction. It was partly gelatinous and mucous, partly fibrous, and partly calcareous. It extended far into the sphenoid and basilar bones and entered the sphenoidal sinuses across the maxilla. Total removal as obviously impossible. The large raw bed of the tumor closed considerably secretating the insertion of muscle flaps.

Histologic report: The operative specimens had the structure of an osteochondromatous mass of modern cellular type.

Except for mild superficial wound infection, which healed under sulfathiazole treatment, the patient made good recovery and as discharged 30 days after operation. Pain, nausea, vomiting and photophobia had ceased completely. Visual acuity improved to 20. There was complete anisometropia in the first and second divisions of the right trigeminal nerve and the total ophthalmoplegia persisted.

Postoperative röntgenograms showed the extensive erosion of the base of the skull to better advantage than the preoperative films. A few residual calcifications were still visible in the left side of the sphenoid body. When the patient as examined last, 6 months after operation, there was evidence of further progression of the lesion. Vision of the left eye as failing and there as left supra-temporal quadrantic defect of the left visual field. Röntgenograms revealed recurrence and further extension of the intracranial calcification.

In the following case the intracranial chondroma was a manifestation of generalized chondromatosis.

Case 5. Gordon H. P. U. of Michigan Hospital, No. 55763, male aged 3 years, as referred by Dr. Joseph Jackson, Michigan. Multiple osteochondromas of right leg and pelvis had been present for more than 3 years. There had been present seasonal syndromes of 6 months duration, the intracranial and retroreticular calcification. Frontal osteoplastic craniotomy with partial removal of retroreticular osteochondroma as performed. Death as occurred outside of the hospital, 6 months after operation.

Autopsy as performed. The patient sustained pathological fracture of the right femur at the age of 5 years. A peculiar swelling developed at the distal part of the right tibia when he was 8 years old. One year later pain and swelling occurred at the old fracture site. Examination then (1910) showed bony hard swelling of the proximal portion of the right femur and smaller swellings at the lower end of the right tibia. Röntgenograms revealed extensive areas of bone destruction and pathological calcifications of the pelvis bones, right femoral shaft, head, and tibia. Exploration of the lower end of the femur disclosed central osteochondroma. After implantation of bone graft, the patient recovered and as not heard of until 3 years later. Six months prior to admission, he noticed progressive failure of vision of the right eye and later similar involvement of the left eye.

Examination revealed multiple chondromas of the right leg. This leg as shortened, due to the old femoral fracture. There were also multiple osseous hyperostoses of the oral cavity. Neurologic signs as confined to changes of the optic paths. Visual acuity as reduced to 6/30, left eye, and 6/60, right eye. The visual fields showed bilateral central scotomata and tendency to be temporal hemianopia. The suprapapillary congestion was distinct. Both optic discs were abnormally pale.

Röntgenograms of the skull revealed erosion of the anterior and posterior clinoid processes, basal enlargement. There were areas of dense calcification in the sella extending to the retroreticular and left parasellar regions.

Diagnosis: An intracranial and retroreticular chondroma as suspected. The chondromas of the right leg, eye, and oral cavity as considered as independent lesions.

Operation as performed on August 24, 1914, under ethyl anesthesia, by Dr. M. V. Frost. A right-sided osteoplastic flap as turned and the chiasmatic region was exposed. The lesion as found to be detached entirely by an encapsulated extradural tumor. After incision of the capsule gelatinous brownish tissue as removed piecemeal. The specimen secured original from the posterior clinoid processes. Its total removal proved to be impossible.

Histologic report: The tumor was a chondroma. The specimen also contained some fragments of normal anterior pituitary lobe.

Although there was no immediate improvement of vision, the patient made a seemingly uneventful recovery and was discharged from the hospital, 25 days after operation. A week later, however, the patient's mother described his condition as "extremely weak" and shortly thereafter his death was reported by the referring physician. No autopsy was obtained. It was suspected that this patient might have died from postoperative cachexia hypophysopriva.

*Primarily extracranial osteochondromas of the ethmoidal or sphenoidal regions with secondary intracranial extension*

CASE 6. Claire C., U of Michigan Hospital, No 425277, female, aged 37 years, was referred by Dr C. King, Toledo, Ohio. Patient presented an osteochondroma of the left maxillary antrum, floor of orbit, and ethmoid, of 17 years' duration. First evidence of intracranial involvement was 7 years after onset, definite signs of right parietal lesion appeared a year later. Trigeminal rhizotomy was done for intractable pain. Extensive extradural and intradural spread of neoplasm noted at the base of the skull. Patient is still alive 17 years after onset, with multiple cranial nerve palsies.

In 1923, 13 years prior to admission, an osteochondroma was removed from the left maxillary antrum, the tumor had invaded the floor of the orbit and the ethmoid cells. Vision of the left eye failed shortly after operation. Six years later (1931) a recurrent tumor was removed from the ethmoid and sphenoid sinuses and deep x-ray therapy was given. A year later (1932) roentgenograms of the skull showed for the first time erosion of the right anterior clinoid process indicative of intracranial extension. In the following year (1933) roentgenograms showed destruction of the posterior wall of the right orbit (major sphenoidal wing) and right parasellar erosion and calcification. Two years later (1935), sclerotic and proliferative changes were noted in the sphenoid body and at the roof of the nasopharynx. There was also involvement of the right frontal and maxillary sinuses. In 1937 one year prior to admission vision of the right eye declined gradually. One month before entrance, severe trigeminal pains developed involving mainly the right second division.

Examination revealed the following: The dilated right pupil reacted hardly to light, the left pupil showed sluggish response. Vision was markedly reduced bilaterally (on the left due to vitreous opacities). The right fundus was normal, the left one could not be seen. Except for corneal areflexia on the right, there was no other trigeminal involvement.

Roentgenograms of the skull revealed extensive destruction and bony proliferation of the sphenoid body (Fig 4, a) ethmoid cells, and all other paranasal sinuses. There were erosion and intracranial calcifications in the right parasellar region.

Diagnosis: Recurrent osteochondroma of the paranasal sinuses with involvement of the base of the skull and intracranial extension to the right parasellar area. It was decided to relieve the patient's pain by trigeminal rhizotomy.

Operation was performed on July 29, 1938, under local anesthesia by Dr M. M. Peet. The region of the right gasserian ganglion was exposed by the usual subtemporal extradural approach. When the trigeminal sheath was opened, the ganglion was found to be surrounded by gelatinous tumor. The basilar dura was then widely opened and the exploration carried far anteriorly and posteriorly. There was diffuse intradural as well as extradural infiltration of tumor from the posterior to the anterior base where the neoplasm was largest. Approximately

30 grams of neoplastic tissue was removed. The entire gasserian ganglion and the adjoining motor root were resected.

Histologic report: The specimen showed an osteochondroma with locally infiltrative tendency. The gasserian ganglion was surrounded, but not invaded, by tumor (Fig 5, c).

Following operation the patient was free from pain. There was not only total sensory and motor trigeminal paralysis but also complete external and internal ophthalmoplegia and blindness on the right. Subsequently, the patient was repeatedly reexamined. The paralysis of the right 2d to 6th cranial nerves remained unchanged. Two years after operation she developed right-sided otitis media and dacryocystitis. Six months later, January 14, 1941, a right Caldwell-Luc operation was performed and tumor of the right maxillary antrum was found to extend into the orbit, ethmoid, lateral wall of nose and petrous-sellar region. After this intervention, transitory cerebrospinal rhinorrhea with signs of meningeal irritation developed, but this subsided after sulfanilamide therapy. The patient returned to the hospital in July, 1942, complaining of severe right temporal headaches. Examination revealed no change in her neurologic and roentgenographic findings but reexploration disclosed a recurrent tumor and a small subtemporal epidural abscess which apparently originated from a chronic otitis media. The entire observed duration of the disease was more than 17 years.

CASE 7. Dagmar T., U of Michigan Hospital, No 306608, female, aged 20 years, was referred by Dr K. B. Babcock, Detroit, Michigan. Patient had an osteochondroma of the left frontoethmoidal region, with 4 months' history. Operation was done with apparently total removal of tumor spreading to the anterior cranial fossa and paranasal sinuses. Small subcutaneous recurrence was removed 4 months later. There were signs of intracranial recurrence after 3 months. A third operation revealed sarcomatous recurrence infiltrating the scalp, dura and brain with extension to the nasal cavity. Death resulted from meningitis, 1 month after last operation. No autopsy was performed.

Four months prior to admission, the patient noticed a swelling on the left side of the forehead which was associated with dull headache, and later on, with diplopia. Biopsy of the lesion elsewhere showed the tumor to be a chondroma. After deep x-ray therapy, the neoplasm began to grow more rapidly.

Examination showed the following: There was a tumor the size of an orange at the left side of the forehead, supraorbital ridge and bridge of the nose. The mass which had the consistency of hard rubber, was firmly attached to its bony base. The overlying skin was intact and not tender to pressure. The tumor displaced the left eye downward and outward, and caused slight edema of the left upper lid. There was also exophthalmos on the left (left eye 20 millimeters, right eye 13 millimeters). The left superior rectus and inferior oblique were paretic. Examination of the left fundus revealed retinal detachment in the region of the superior temporal vessels and venous engorgement.

Roentgenograms of the skull revealed a neoplasm eroding the left frontal bone, the frontal sinuses (especially the left one), the ethmoids and the roof and medial wall of the left orbit. Extensive calcifications were present within the tumor (Figs 4, b and c).

Diagnosis: Osteochondroma (or osteochondrosarcoma) of the left frontal and ethmoidal bones with intranasal, orbital and intracranial extension.

Operation was performed on April 14, 1933, under ether anesthesia by Dr M. M. Peet. After a large frontal scalp





Fig. 6. Histological sections from malignant osteochondroma, Case 7. a, left, Specimen from first operation shows relatively benign osteochondroma. b, Specimen of recurrent tumor obtained by third operation, shows sarcomatous change (osteochondrosarcoma.)

flap had been turned down, lobulated bluish tumor as exposed, covered by pericranium. The lower portions of the frontal bone are resected away to further expose the neoplasm, which completely filled the frontal sinuses. On the left side, the tumor had destroyed the frontal bone, forming large mass outside and still larger mass inside of the bone displacing the dura posteriorly. The neoplasm as firmly attached to and infiltrating the cribriform plate and extended into the ethmoid cells. The inner walls of both orbits are involved, especially on the left. After removal of all visible tumor, the widely opened nasal cavity was closed by an iodoform pack. A tear of the orbital dura back could not be sutured had to be covered by another iodoform pack.

**Histologic report.** The tumor as an osteochondroma with calcareous concretions in myxomatous stroma. The neoplasm was regarded as not sufficiently cellular to cause metastases, but likely to recur and infiltrate locally (Fig. 6).

The postoperative course as complicated by transient cerebral spinal rhinorrhea and by severe epistaxis, both as eventually controlled by ligation of the left external carotid artery.

The patient returned to the hospital 4 months later with recurrent tumor. A neoplasm, the size of a fist, had infiltrated the skin as well as the dura, as removed. Histologic examination showed that the growth had become increasingly cellular and had penetrated the dura, and that the involved portion of the skin contained no connective tissue. Thereupon the patient as given course of deep x-ray therapy (500r).

Three months thereafter she returned with gross intracranial recurrence and was again operated upon by Dr. Peet on November 5, 1913. The recurrent tumor infiltrated the skin, dura and frontal lobes and had ex-

tended far into the nasal cavity. It as moved higher with the tumor-infiltrated skin, dura, and frontal cortex. The skull as packed and only partially healed. It was hoped that the large defect could eventually heal by granulation. Patient did fairly well for 3 years, but then developed meningitis leading to her death on December 11, 1915, approximately 1 year after the onset of the disease. Autopsy as not obtained.

The last surgical specimen showed that the neoplasm had become definitely sarcomatous in character (Fig. 6b).

#### ANATOMICAL AND PATHOGENETIC CONSIDERATIONS

From the observations here noted and the cases reported in the literature it is evident that the base of the skull is preferential location of osteochondromas. When verified by operation or a autopsy these tumors often are found to be so large that it may be difficult or even impossible to ascertain their exact site of origin, yet the clinical course may be helpful in reconstructing the stages of anatomic evolution even in advanced cases.

In the first group, *primarily sphenoidal in origin*, there are 5 examples in our series. Four of these (Cases 1, 2, 3 and 4) are almost identical with the four observations reported by Hirschfeld, Levitt, Green and Childrey and Paley. In all 5 instances the osteochondroma originated from the sphenoid bone and protruded intracranially

in the posterior parasellar region. It was attached to one side of the clivus and the corresponding posterior clinoid process (Fig 3, a) and spread to the base of the greater sphenoidal wing and adjacent bone by expansion rather than by actual invasion (Case 3). At first, the growth was entirely extradural, but later it protruded into the cranial cavity by penetrating the dura (Case 1). Leptomeninges and brain were indented and displaced, but not invaded.

The fifth case in our first group (Case 5) must be given special consideration since the basal osteochondroma was but one manifestation of generalized chondromatosis. There are two similar observations recorded in the literature (Clark, Lupo), but the validity of these appears dubious, because they were not verified. The objection might be raised here that localization at the base of the skull is merely incidental in general chondromatosis, yet it cannot be overlooked that in all 3 instances the chondroma of the sphenoid represented the only cranial localization.

In the second group, *primarily extracranial tumors*, there are 2 examples in our series (Cases 6 and 7). In these 2 cases, and in similar observations reported by Torrigiani, Wolf and Echlin, Menne and Frank, and others, the tumor arose in the sphenoidal or ethmoidal region and developed mainly in an extracranial direction, at an advanced stage, however, it also invaded the cranial cavity. Thus in Case 6, the osteochondroma presumably originated unilaterally in the posterior parts of the ethmoid and was first detected in the corresponding maxillary antrum. Later on the neoplasm spread through the ethmoidal cells and sphenoidal sinus to the other side where it penetrated the base of the skull in the parasellar area. Case 7 is an example of a more anteriorly placed lesion which developed in the frontoethmoidal area and invaded the orbit, the upper parts of the nasal cavity, and the floor of the anterior cranial fossa. In this instance the malignant (sarcomatous) character of the lesion was demonstrated by infiltration of scalp and brain. A similar case was described by Menne and Frank. In Torrigiani's patient the chondroma apparently originated in the sphenoidal sinus and extended intracranially, thus destroying the sella turcica. Wolf and Echlin briefly mention an observation at autopsy of a large chondroma of the sphenoidal region, extending into the nasopharynx.

The pathogenesis of basal osteochondromas is revealed by their characteristic site. It is highly probable that these tumors develop from residuals of the cartilaginous primordial cranium. Embryonic cartilaginous rests with future neoplastic

propensities may be retained, either in suture lines or in areas between centers of ossification. Thus, one may expect foci of neoplastic growth at the junction of the sphenoid body with the greater wing of the sphenoid and petrous apex (Cases 1, 2, 3, and 4), or at the junction of the ethmoid with the sphenoid body (Case 6), or at the frontoethmoidal border (Case 7). It is also conceivable that chondromas may arise from heterotopic cartilaginous material within the mucous membranes of the paranasal sinuses.

The pathogenesis of basal osteochondromas should not be discussed without mentioning their relationship to the chordomas. The latter variety of tumor is derived from the notochord, a forerunner of the embryonic (cartilaginous) axial skeleton. It is interesting to note that chordomas are found in a location similar to that of osteochondromas, viz at the junction of the basisphenoid with the basiocciput.

The histologic picture of basal osteochondromas is generally characteristic, although it may exhibit considerable variations. Some neoplasms are almost entirely composed of mature cartilage (chondroma), others contain elements of adult or embryonic mesenchymal tissue (fibrochondroma, myxochondroma, respectively) (Fig 5, b). As a rule, areas of ossification are present (osteochondroma—Figs 5, a and 5, c) and also degenerative changes such as calcification or mucinous degeneration. Some chondromas are acellular and noninfiltrative, others are highly cellular, poorly differentiated, and grow in a malignant fashion (chondrosarcoma—Case 7). Occasionally, a relatively benign osteochondroma may undergo progressive anaplastic differentiation into a malignant osteochondrosarcoma (Case 7, Figs 6, a and b).

#### CLINICAL AND DIAGNOSTIC CONSIDERATIONS

*Incidence and duration of symptoms.* Basilar osteochondromas occur possibly more often in the female sex, but the number of observations is too small to permit accurate statistical evaluation. As a rule, these neoplasms become clinically manifest in young adults, between the ages of 20 and 30. Their rate of growth is slow, hence a clinical course over 10 or even 20 years is not unusual. If, on the other hand, the tumor becomes malignant, the course is likely to be rapid (1 year in Case 7).

*Neurologic symptomatology.* The intracranial osteochondroma of the sphenoid produces a characteristic clinical syndrome. As a result of the parasellar location of the lesion, the structures in the wall of the cavernous sinus are affected at an

early stage. Paralysis of the 3d, 4th, 5th, and 6th cranial nerves are nearly always demonstrable. The lesion of the oculomotor nerve may remain incomplete and spare the medial rectus and the levator palpebrae superioris. Neuralgic pains in the distribution of the ophthalmic division and diminution of corneal reflex are early signs of trigeminal involvement. Sensory loss is usually most marked in the first trigeminal division and least in the third division, but when the tumor has attained a large size and compresses the gasserian ganglion, all trigeminal branches including the motor root may be equally affected. Sharp trigeminal pains should be differentiated from the duller and throbbing headaches elicited by irritation of the highly sensitive dura of the base and the cavernous sinuses. This dull pain is referred to the ipsilateral forehead, temple, occiput, and behind the eye. Its frequent association with nausea and vomiting (in Case 4) probably is a local meningeovagral reflex phenomenon and should not be interpreted as evidence of increased intracranial pressure. In fact, basal osteochondromas rarely produce definite signs of increased intracranial pressure and if so, only in the advanced stage. This is explained by the slow growth rate and the extradural location of these neoplasms. Since venous return to the cavernous sinuses is mechanically impaired by the tumor thrombotic processes may occur an event which is indicated by sudden increase of cranial nerve involvement: exophthalmos, local edema, and venous stasis of eyelids. Sooner or later the optic pathway also becomes implicated. Depending upon the direction of neoplastic growth, optic nerve, chiasm, or optic tract may suffer from local pressure. In more anteriorly placed lesions, a chiasmal syndrome with optic atrophy is likely to develop at an early stage (Case 5). In tumors extending more posteriorly and upward homonymous hemianopia, due to compression of the optic tract, may result (Case 1). Large osteochondromas inevitably encroach upon the hypothalamus and its stalk, the hypothalamic region, the medial portion of the temporal lobe and the cerebral peduncle. Correspondingly a pituitary hypothalamic syndrome may develop and can be recognized by the presence of obesity, polyuria, polydipsia, impotence, or amenorrhea, and drowsiness (as in Case 1 and in the observations of Pabeani and Torrigiani). In two of our observations (Cases 2 and 3) peculiar attacks were noted, characterized by vegetative (parasympathetic) phenomena, indescribable sensation of fear without lowering of consciousness. These seizures might have been convulsive equivalents and

evoked either by hypothalamic stimulation (astonomic epilepsy?) or perhaps by hippocampal discharge (atypical uncinate attacks?). Signs referable to compression of the cerebral peduncles are usually slight and clinically recognizable by minimal contralateral hemiparesis with increased deep reflexes. At an advanced stage, the expanding osteochondroma extends through the inferior tentorium into the posterior fossa causing paresis of the 7th and 8th cranial nerves (Cases 2 and 3).

Primarily extracranial osteochondromas of the ethmoidal or sphenoidal regions produce neurologic signs only in the later phases of the disease. At first, the symptomatology is rather uncharacteristic and indicative of an expansive or obstructive lesion of the paranasal sinuses. The neoplasm may become directly visible by rhinoscopy. Metastases, infections of the occluded sinuses, dacryocystitis and orbital cellulitis are occasional complications which obscure the clinical picture. If the tumor invades the orbit, the eye bulges and is displaced downward and outward, thus accounting for diplopia and blurred vision. When the neoplasm finally penetrates into the cranial cavity the optic nerve is the first structure to be come affected. This is manifested by signs of retrobulbar neuritis and, later by optic atrophy and blindness. Posterior extension of the tumor through the pterygopalatine foram and superior orbital fissure toward the parasellar region produce involvement of the 3d, 4th, 5th (first and second divisions) and 6th cranial nerves.

**Radiographic signs.** The presence of basal osteochondromas is revealed by localized erosion of bone combined with dense calcifications in the tumor (Figs. 2, 3 and 4). Intracranial sphenoidal osteochondromas produce more or less marked parasellar erosion, i.e., unilateral destruction or thinning of clinoid processes, and sometimes also erosion of the medial portion of the lesser sphenoidal wing and of the petrous apex (Cases 3 and 4). Ethmoidal osteochondromas may destroy ethmoidal bones, the floor of the anterior fossa, and the medial wall of the orbit (Case 7). Calcifications in osteochondromas are either arranged in coarse flakes (Figs. 1, a, b and 4, b, c) or they may be so dense as to simulate cancellous bone thus outlining the entire tumor mass (Figs. 2, a, b).

**Diagnosis.** The diagnosis of osteochondroma arising from the base of the skull can be made before operation. Since parasellar lesions produce a characteristic clinical syndrome they can be accurately localized, but it may be more difficult to ascertain the pathological type of the lesion present. The following conditions must be differentiated from the osteochondroma:

1 The subclinoid (parasellar) aneurysm of the internal carotid artery may be associated with similar neurologic signs,<sup>1</sup> but its history is usually shorter and the onset of symptoms more abrupt, furthermore it is likely to occur in older individuals. Calcified aneurysms show smooth round contours, sometimes only a semicircular line of calcification. The differential diagnosis can be made with certainty by arteriography.

2 Parasellar meningiomas, arising either from the anterior clinoid process, lateral wall of cavernous sinus or gasserian sheath ("gasseropetrosal meningiomas") are apt to cause earlier and more marked visual changes. Meningiomas of the inner portion of the lesser sphenoidal wing and anterior clinoid process produce early ipsilateral optic atrophy with visual field changes, later on a Foster Kennedy syndrome, gasseropetrosal tumors cause bilateral papilledema. Basal meningiomas often show localized hyperostoses at the point of their attachment, but they are less frequently calcified than chondromas. Calcareous shadows in meningiomas are usually finer and more uniform than those present in osteochondromas.

3 Craniopharyngiomas occur in patients of a younger age than do osteochondromas. They nearly always affect the optic pathways and the hypophyseal-hypothalamic area, and commonly produce signs of increased intracranial pressure, but encroach less often on other cranial nerves. Roentgenologically, they are characterized by intrasellar or extrasellar, but not parasellar erosion and by fine granular intrasellar or suprasellar calcifications which, as a rule, lie in the midline.

4 Chordomas may exhibit a symptomatology resembling that of osteochondromas. Their course is shorter, however, with a greater tendency to affect cranial nerves bilaterally and to invade the posterior fossa. These tumors may lead to considerable destruction of bone but do not calcify.

Primarily extracranial osteochondromas cannot be differentiated clinically from other neoplasms invading the base of the skull and paranasal sinuses, but their characteristic roentgenographic appearance may permit an anatomic diagnosis.

#### TREATMENT AND PROGNOSIS

*Treatment* Since osteochondromas do not respond to radiation, surgical treatment is the only promising form of therapy. Primarily intracranial osteochondromas must be dealt with by

neurosurgical methods. Unfortunately, it is rather difficult to expose the posterior parasellar region from which most of these tumors arise. An extradural subtemporal approach, as is customary in trigeminal rhizotomy, rarely affords sufficient exposure, unless the lesion is small. The usual exploration of the pituitary region by a frontal osteoplastic flap is likewise inadequate, since it permits inspection only of the anterior parasellar area. Much better access to the parasellar region is obtained by a low frontotemporal osteoplastic craniotomy combined with subtemporal decompression. Since intracranial pressure is usually not high, the outer margin of the lesion may be disclosed by intradural elevation of the temporal lobe, but hardly sufficient room is obtained in this manner for safe and complete removal of the neoplasm. It is, therefore, advisable to resect the anterior and inferior parts of the temporal lobe to uncover the deep seated tumor (Figs 3, b and c). Technical difficulties of the operation are caused by the extradural and intradural expansion of the tumor, and by its intimate relationship to various cranial nerves, cavernous sinus, and to the internal carotid artery. Although the neoplasm itself may be completely avascular, detachment from its base may cause considerable hemorrhage, mostly from the middle meningeal artery and from venous radicals of the cavernous sinus and superior petrosal sinus. Most osteochondromas are easily broken up during removal, due to their brittle consistency. This facilitates their piecemeal removal, but it also increases the likelihood of incomplete extirpation. It is almost unavoidable that attempted radical removal of these tumors should be followed by at least a temporary increase of cranial nerve palsies (Cases 1, 2, and 3).

In primarily extracranial osteochondromas of the ethmoid of sphenoid, rhinologic methods of treatment are indicated and complete eradication possible, as long as they are small and confined to the paranasal sinuses. Large neoplasms, however, with extensive involvement of the orbit and intracranial cavity offer a very poor operative prospect. Combined intracranial and nasal approach was attempted in Case 7 and afforded a good exposure of the lesion. It should be mentioned that such an operation inevitably establishes a wide communication between the nasal and intracranial cavities with all its dangerous consequences, such as postoperative cerebrospinal rhinorrhea and ascending meningeal infection. On the other hand, the use of sulfonamides has considerably lessened the peril of these dreaded complications at the present time.

<sup>1</sup>In Case 4 the lesion was mistaken for an aneurysm before definite changes were visible in the roentgenogram.



# THE RESULTS OF NEPHRECTOMY ON EXPERIMENTAL RENAL HYPERTENSION

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**D**URING the past 6 years there has been considerable interest in the relationship between unilateral renal disease and arterial hypertension in man, and numerous efforts have been made to modify that hypertension by removal of the diseased kidney. Undoubtedly the impetus for this clinical approach has been the studies of experimental renal hypertension initiated by Goldblatt and his group who demonstrated that permanent hypertension results from interference to the renal blood supply. Shortly afterward, scattered case reports appeared in which nephrectomy was followed by a cure of the hypertension. Subsequent reports by urologists have been numerous and the results variable. In 1941, Abeshouse (1), in an extensive review, summarized the literature on hypertension and unilateral renal disease.

## REPORTED CLINICAL RESULTS

Using part of this collected data (2), we have prepared a table showing the end-results of nephrectomy on those forms of hypertension presumably originating from a single diseased kidney. This is not a complete compilation of all reported cases, but represents a very large sampling.

Table I presents the type of unilateral renal disease associated with hypertension and the number of cases studied after unilateral nephrectomy. The results are tabulated under 3 headings which might be termed in effect "failures," "improved," and "cured." It is evident at first glance that the results vary according to the type of kidney disease. It is not statistically sound to present totals on such a miscellaneous collection of cases, nevertheless, such totals give an indication of the trend of the results obtained and furthermore enable us to compare the clinical results with the experimental results which we present below. It will be noted that approximately one-fourth of all of the reported cases resulted in a complete relief of the arterial hypertension, but that in over

half of the cases there was either no lowering of blood pressure or a continuation of the rise following extirpation of the diseased kidney.

A few of the failures may be due to the fact that the hypertension was independent of the renal disease, in others there may have been a coexisting disturbance of circulation in the remaining kidney. Furthermore, even though the remaining kidney was shown to be normal by the usual kidney function tests and appeared to be normal following a thorough urological study, it is recognized that experimental renal hypertension may exist in animals with normal clearance values (6) and that there may be "silent" parenchymal renal lesions in man. In the majority of instances the residual hypertension following removal of the diseased kidney has been unexplained.

## EXPERIMENTAL INVESTIGATION

Our experiments were designed to answer several questions bearing upon this problem: (1) In hypertension produced experimentally by unilateral partial ligation of the renal artery, what are the end-results of removing the affected kidney and how do these results compare with the clinical reports? (2) What are the factors that determine the success or failure of nephrectomy in curing the hypertension? (3) Does the hypertension resulting from the unilateral disease produce irreversible changes in the opposite kidney? (4) If so, is it the severity of the hypertension or its duration that causes the greatest damage?

The rat, sheep, and goat are the only known species except for man in which unilateral renal damage may result in permanent hypertension. Unlike dogs, rabbits, and monkeys, in which unilateral renal ischemia produces a transient hypertension only, some of our observed rats with unilateral partial renal artery ligation have had a permanent hypertension for a year and a half, and this period of time represents over half of the usual lifetime of the animal. For these reasons, the rat was chosen for our experimental observations.

**Methods** In young adult rats of both sexes the left renal artery was partially occluded by a silk

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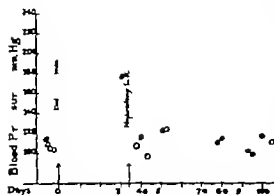


Fig. Complete relief of hypertension of short duration.

ligature the technique of Wilson and Byrom being used (13). Blood pressures were followed two or three times a week by the tail plethysmograph method of Williams, Harrison and Grollman. After the hypertension had developed and was moderately well stabilized the left kidney was removed and the blood pressure followed for a period of several weeks. The excised kidney was preserved in Bouin's fluid for histological study. In many animals the quantitative urinary output of albumin was checked before and after the nephrectomy. The animal was finally sacrificed, the weight of the heart obtained, and various tissues saved for a histological study of the vascular system.

**Results.** The initial preoperative blood pressures of our normal rats ranged from 100 to 120

with a mean of 110. We considered any rat hypertensive when two or more consecutive readings were over 140 millimeters or in which the average value of all of the readings following the operation was over 130 millimeters. In the study of several hundred rats, we have never found a sustained spontaneous hypertension. Some of the animals we operated upon developed a hypertension of over 200 millimeters systolic pressure.

Table II shows the results of the nephrectomy in relation to the duration of the hypertension and also in relation to its severity. The severity of the hypertension had little to do with the success of the nephrectomy, but the duration did. Any level of hypertension of less than 100 mm. was usually markedly improved or reduced to normal by removal of the affected kidney. Two weeks in the life of a rat is roughly comparable to 1 year in man.

Charts 1, 2 and 3 illustrate sample protocols on typical experiments.

Two groups of independent workers have recently reported similar observations on rats. Wilson and Byrom (14) produced hypertension in 27 rats by applying a small silver clip to one renal artery, and they studied the results of removing that kidney. Friedman, Jarman, and Klempner (5) applied a cellophane bag to one kidney thus producing a perinephritis and this resulted in sustained hypertension in a group of 44 rats. Table III presents a summary of all of the reported results.

In spite of differences in technique it will be noted that the results are similar. The totals are

TABLE I.—THE THERAPEUTIC EFFECTIVENESS OF NEPHRECTOMY IN CLINICAL HYPERTENSION

Type of unilateral renal disease associated with hypertension	Number of patients having nephrectomy	Effect on hypertension			
		No change or rise	Definite lowering (but not to normal)	Sustained return normal	
				No.	Per cent
Pyelonephritis	41	14			38
Tuberculosis	18			10	56
Chronic inflammatory disease complicated by calcosis	11	87		20	26
Unilateral hydronephrosis	38				37
Nephrosis	41				
Congenital hypoplasia of one kidney					100
Totals	111	23	23	20	
Per cent		60	20	20	

TABLE II.—THE RELATION OF DURATION AND SEVERITY OF HYPERTENSION TO THE EFFECTIVENESS OF NEPHRECTOMY IN RATS

Duration—wks.	No. of animals	Result of nephrectomy		
		No change or rise	Lowered, but not to normal	Returned normal
1-10	11			
11-20	26			
Totals	47	13	20	
Severity of hypertension—mm.				
140-200	26	13		
201-250	13			
251-300				
Over 300				
Totals	47	13	20	

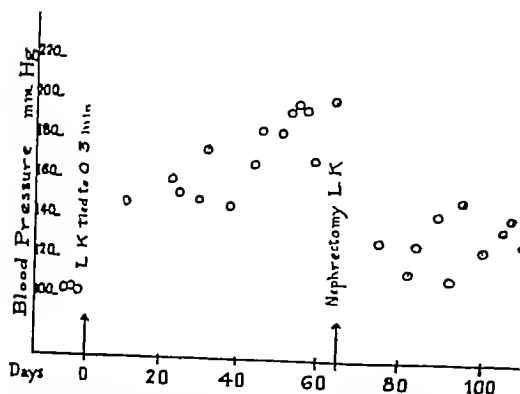


Fig 2 Moderate improvement of hypertension of 2 months' duration

presented in Table III and the very close similarity between the results obtained by nephrectomy in all the clinical cases reported (compare with Table I) and the results obtained by nephrectomy in hypertensive rats by three groups of workers would seem to indicate that the nature of the residual hypertension in both rats and in man is the same. Thirty per cent of human cases and 29 per cent of rats were completely relieved by nephrectomy.

We observed one interesting fact which is readily explained. In some of the animals, the left kidney to which the blood supply had been reduced by operation became progressively atrophied until at the time of its removal there was nothing left but a small calcified nodule. Removal of this mass did not lower the hypertension in a single instance. These nodules had once been small, pale kidneys which secreted the renal pressor substance and caused hypertension and, in turn, had resulted in damage to the opposite kidney. If subsequent atrophy with complete loss of blood supply to the affected kidney failed to cure the hypertension, it is obvious that surgical nephrectomy would accomplish no more. In other rats even though the renal artery was found to be completely occluded, there was a small pink area at the inferior pole of the kidney supplied by the spermatic or ovarian branch of the ureteral artery, and nephrectomy in these animals often lowered the blood pressure.

**Pathological observations** During life, large amounts of albumin were excreted by the hypertensive rats, but the amounts did not parallel the severity of hypertension. Following nephrectomy, there was no consistent change in the albuminuria, indicating that most of the protein leaked through the glomeruli of the intact kidney.

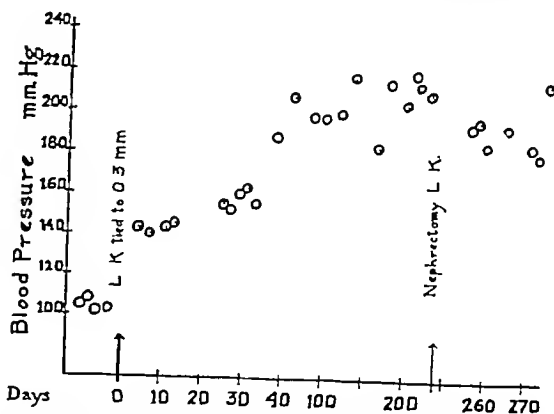


Fig 3 No lowering of hypertension of 7 months' duration (Time scale has been altered to conserve space.)

Cardiac enlargement, from 10 to 50 per cent above the expected weight, was observed on all rats still hypertensive at the time of death. The increase in heart weight was quite closely proportional to the level of blood pressure at the time of death. In view of the invariability with which such enlargement is noted, it is interesting to observe that the heart weight was normal in those rats "cured" by nephrectomy, even though the blood pressure had once been at very high levels. This establishes the reversibility of cardiac hypertrophy.

Histological examination of the kidneys<sup>1</sup> showed a number of pathological changes similar to those seen in human hypertensive disease. In the left kidneys which had been removed surgically, there

<sup>1</sup>We are indebted to Mr. E. Johnson and Mr. R. Bazzanella for preparation and special staining techniques and to Dr. David Singman for interpretation of the renal changes.

TABLE III—COLLECTED RESULTS OF NEPHRECTOMY ON EXPERIMENTAL HYPERTENSION IN RATS

Authors	Method of producing hypertension	Number	Result of nephrectomy		
			No change or a rise	Lowered but not to normal	Return to normal
Wilson and Byrom	Silver clip obstructing one renal artery	27	8	9	10
Friedman, Jarman and Klempner	Cellophane bag around one kidney	44	3	20	12
Patton, Page and Ogden	Partial occlusion with silk tie of one renal artery	47	15	20	12
Totals		118	26	39	24
Per cent			22	33	20



were large areas of necrosis due to anemic infarction together with relatively normal appearing tissue. The iron hematoxylin and aniline blue stain revealed varying degrees of thickening of the glomerular capillaries. In some instances, there was a thickening of the arterioles, but in general the vascular changes in the ischemic kidney were not as marked as in the intact kidney.

The right kidneys, which had not been disturbed surgically, showed a varying degree of thickening of the walls of the arterioles with increased cellularity in all instances. There were no arteriosclerotic changes noted in the larger arteries. The parenchyma showed tubular dilatation and cloudy swelling. The glomerular capsules appeared thickened, and the glomeruli were quite cellular and showed a thickening of the capillary walls such as noted in cases of human eclampsia (8). In addition to the vascular changes, there were varying degrees of interstitial inflammation in some of the nonligated kidneys.

The pathological changes observed in these kidneys are quite identical with those described and illustrated by Schroeder and Neumann (10) who likewise studied the effects of arterial hypertension in rats. We agree with them, as opposed to the findings of Wilson and Byrom (5) that the kidney to which the blood supply was limited participates in the vascular changes. This may simply indicate that the meso-intrarenal arterial pressure—apart from the pulse pressure—is the same on both sides in spite of the renal artery constriction.

#### EVALUATION OF STUDY

Our findings confirm the opinions of Welas and Parker and of Wilson and Byrom (14) that unilateral renal disease sets up a vicious circle resulting in irreversible damage to the opposite kidney which then results in further hypertension, further renal damage, and so on.

In order to cure experimental renal hypertension in rats by nephrectomy the disease should be of short duration and the renal lesion must be confined to one kidney but must not have produced a total lack of function of that kidney. These criteria are similar to those derived from clinical observations on man by Schroeder and Flah (9) who set an arbitrary limit of 3 or 5 years for the duration of human hypertension if a satisfactory result from nephrectomy were to be expected. It is of interest that this period corresponds roughly to the percentage of life span which also holds true in rats. It seems that the rate of development of such pathological changes in the vascular system of rats is markedly accelerated.

As stated in a recent study of 103 nephrectomized patients by B. Friedman Mochowitz, and Marrus (4) the decision to remove a pathological kidney should be based on the nature of the disease and not on the expectation of curing hypertension. If the opposite kidney were unexpectedly diseased, the nephrectomy might indeed precipitate a further increase in blood pressure. In 5 carefully studied cases, M. Friedman and his co-workers (5) determined the diastolic and final clearance before and after unilateral nephrectomy and in 3 cases demonstrated the feasibility of separate renal clearance determinations for each kidney. Unless this separate evaluation is done, no function test would furnish a positive clue as to the presence or absence of unilateral kidney disease.

Whether the damage to the normal kidney resulting in residual hypertension is caused by the hypertension *per se*, or by a toxic substance arising from the diseased kidney as suggested by the work of Winternitz is not clear and our data sheds no light on this problem. The often confirmed observation that residual hypertension following the acute hypertensive states of pre-eclampsia and eclampsia depends more on the duration than the severity of the disease coincides with our conclusions.

#### SUMMARY AND CONCLUSIONS

The reported clinical cases of hypertension and unilateral renal disease in which a nephrectomy was done have been reviewed. In over half of these patients the blood pressure was not lowered or continued to rise following surgery.

This problem was studied on rats in order to determine the factors which influence the success or failure of nephrectomy in curing hypertension. Permanent high blood pressure was produced by obstructing the blood supply to one kidney and this kidney was then removed after varying intervals of time. Like the results in man, half of our rats had no lowering of the blood pressure and only 20 to 30 per cent of the animals were cured of hypertension. In the animals with residual hypertension, albuminuria persisted, and a histological study of the remaining kidney revealed numerous vascular changes similar to those observed in human hypertension and apparently accounting for the continued maintenance of the high blood pressure. If the affected kidney had become completely devoid of a blood supply its removal was a useless procedure. The greatest success following nephrectomy was in those animals with hypertension of short duration, and within the limits of our experiments, the severity of the hypertension was not of importance in determining the end-result.

## REFERENCES

- 1 ABESHOUSE, BENJAMIN S. *Surgery*, 1941, 0 042
- 2 Idem. References 23, 32, 33, 38, 56, 62, 68, 119, 129, 143, 155, 156, 172, 183, 190, 200, 214, 250, 253
- 3 FRIEDMAN, B., JARMAN, J., and KLEMPFNER, P. *Am J M Sc*, 1941, 202 20
- 4 FRIEDMAN, B., MOSCHOWITZ, I., and MARRUS, J. *J Urol.*, 1942, 48 13
- 5 FRIEDMAN, M., SELZER, A., KREUTZMANN, H., and SAMPSON, J. J. *J Clin Invest*, 1942, 21 19
- 6 FRIEDMAN, M., SUGARMAN, H., and SELZER, A. *Am J Physiol*, 1941, 134 403
- 7 GOLDBLATT, H., LYNCH, J., HANZAL, R. F., and SUMMERVILLE, W. J. *Exp M*, 1934, 50 347
- 8 PAGE, F. W., and COX, A. J. *West J Surg*, 1938, 46 463
- 9 SCHROEDER, H. A., and FISH, G. W. *Am J M Sc*, 1930, 190 601
- 10 SCHROEDER, H. A., and NEUMANN, C. J. *Exp M*, 1942, 75 527
- 11 WELLS, S., PARFIER, F., and ROHM, G. P. *Ann Int M*, 1933, 6 1500
- 12 WILLIAMS, J. R. JR., HARRISON, T. R., and GROLLMAN, A. J. *J Clin Invest*, 1930, 18 373
- 13 WILSON, C., and BYROM, I. B. *Lancet*, 1930, 1 156
- 14 Idem. *Q J Med*, Oxf, 1941, 10 65
- 15 WINTERFELT, M. C., MYLON, J., and KATZMAN, R. *Yale J Biol*, 1941, 13 505

# AN IMPROVED OPERATIVE METHOD FOR OBTAINING BONY FUSION OF THE GREAT TOE

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FOR many years it has been the practice on the various services at the Crippled Children's Hospital to carry out an operative fusion of the interphalangeal joint of the great toe in all cases of transplantation of the extensor hallucis tendon to the dorsum of the foot.

It has been observed that bony fusion of this joint actually occurs in only a comparatively small percentage of these cases (Table II). Many patients develop a satisfactory fibrous fusion in good position and are pain free. Many others present no fusion at all, but the toe remains in good position, the handicap being difficulty in putting on socks and shoes due to instability of the toe. A certain other percentage (Table I) however go on to flexion contracture of the toe with definite symptoms caused by resulting hammer toe, namely corns, calluses, and inability to wear a shoe. Many of the patients therefore

From the orthopedic service of the Crippled Children's Hospital.

required a re-fusion of the toe, either because of pain or the inconvenience resulting from instability.

The usual method of arthrodesis of the interphalangeal joint was carried out in the majority of these patients. This procedure consisted of removal of the cartilage, careful approximation of the raw bone surfaces, and suture of the stub of the extensor hallucis attachment to the periosteum of the dorsum of the proximal phalanx. Plaster immobilization was carried out, usually incidental to whatever period of time the foot required immobilization, i.e., triple arthrodesis, some 3 months; tendon transplants, 3 to 6 weeks, etc. No specific fixation was applied other than the cast to the foot. In an analysis of a series of patients which we were able to follow at the clinic, it appeared that about 80 per cent of the patients did not get a bony fusion, and that 20 per cent required re-fusion because of the resultant flexion deformity or other complaints. For this reason, we felt it advisable to seek more certain

TABLE I.—CASES OF GREAT TOE FUSION WITHOUT WIRE FIXATION

No. Age	Initial Sex	Result
30	B. E. M.	Fibrous union with toe flexion deformity
34	B. M.	Fibrous union with toe flexion deformity
	A. E. F.	Fibrous union with toe flexion deformity
	N. C. F.	Fibrous union with toe flexion deformity
3	B. V. M.	Bony union
	W. W. M.	Bony union
1	L. H. F.	Fibrous union
	R. M.	Fibrous union
	N. J. F.	Fibrous union
20	E. D. M.	Fibrous union

No. Age	Initial Sex	Result
14	B. W. M.	Bony union
	C. M.	Fibrous union
20	O. C. M.	Fibrous union
	B. B. M. F.	Fibrous union
10	K. B. M.	Fibrous union
15	L. C. M.	Fibrous union
17	O. J.	Bony union
13	R. M.	Fibrous union
3	C. M.	Bony union
20	S. M.	Fibrous union

\*These toes required re-fusion because of flexion deformity.

Mild post-operative infection, good clinical result.

Diagrams were polyethylene in all cases. Immobilization consisted of plaster cast for 2, 6, 12 weeks, depending on foot operation, i.e. tendon transfer triple, etc.

no post-operative infection, no post-operative flexion deformity.

(All cases included are from the orthopedic service of Crippled Children's Hospital.)



Fig 1 Typical case showing flexion deformity following failure of fusion



Fig 2 Postoperative film, showing position of pin

TABLE II—CASES OF GREAT TOE FUSION WITH INTERNAL WIRE FIXATION

No	Initials	Time	Time	Results
Age	Sex	pin removed	of fusion	(x ray)
1	BS	7 weeks	15 weeks	Bony fusion
10	M*			
2	BB	7 weeks	8 weeks	Bony fusion
16	M*			
3	AR	11 weeks	No fusion	Fibrous union
9	F*			
4	KG	13 weeks	13 weeks	Bony fusion
6	M			
5	WC	10 weeks	12 weeks	Bony fusion
7	F*			
6	LN	7 weeks	16 weeks	Bony fusion
7	F			
7	FB	14 weeks	No fusion	Fibrous union
10	F†			
8	CB	16 weeks	16 weeks	Bony union
0	M			
9	PA	8 weeks	12 weeks	Bony union
10	F			
10	VE	Pin still in	12 weeks	Bony union
17	F			
11	FS	20 weeks	10 weeks	Bony union
13	M			
12	LV	17 weeks	12 weeks	Bony union
10	F†			
13	CP	16 weeks	16 weeks	Bony union
8	M†			
14	DG	12 weeks	18 weeks	Bony union
15	F†			

\*Cases re fused because of flexion deformity following original fusion operation.

†Complicated by infection of the distal phalanx. After curettement good clinical result.

‡Private patients of D H O D

§Diagnosis of all cases was poliomyelitis. Majority of cases from the orthopedic service of Crippled Children's Hospital.

85 per cent had solid bony fusion, 14 per cent, fibrous union no deformity, 7 per cent infection none had flexion deformity



Fig 3 Same case as Figure 2 showing bony union and removal of pin

method for fusion and so prevent this high percentage of poor results

Taylor reported a method of fixation for the phalanx in treatment of hammer toe which seemed highly adaptable to this situation. Our present operative technique follows. Careful denudation of the cartilage surfaces of the interphalangeal joint is carried out with apposition of the raw bone surfaces. While the toe is held in satisfactory position, a Kirschner wire is drilled linearly through the end of the toe, traversing the distal phalanx, crossing the denuded joint, and extending well into the proximal phalanx. Ordinary closure is then carried out. Since the Kirschner wire provides such firm internal fixation, no external immobilization is necessary. Various methods of treatment of the end of the wire have been used, the most satisfactory being to clip it

off just outside of the skin surface. This permits easy removal and at the same time the wire is not left protruding enough to interfere at all with the sock or the shoe. Weight bearing is permitted as soon as the wound is healed, provided other conditions of the foot permit. Following adoption of this method of treatment bony fusion occurred in 85 per cent of the patients (Table II). Three patients developed slight serous drainage about the wire, which promptly healed following removal of the wire. The only complication of any note consisted of a localized osteomyelitis around one of the wires. This occurred when the patient accidentally kicked the wire back into his toe while going barefooted. (The wire had protruded too far.) On removal of the wire and curettement of the sinus, this condition healed promptly without solid fusion of the joint but with good clinical result. In one other patient of this series fusion failed in this particular case; the wire was removed too soon. The patient obtained only fibrous union, but with a satisfactory clinical result. Since there seems to be no contraindication to leaving the wire in, under ordinary circumstances the wire is not usually

removed until bony fusion is demonstrable by x ray. Many of our patients wore the wire even longer than necessary, due to the fact that they were having no difficulty and failed to return to the clinic at the designated time. The average time for leaving the wire in was 12 weeks, and it is probable that a somewhat longer period would be desirable provided there is no discomfort from the wires. All of the patients reported had polio-myelitis and were subjected to a transplantation of the extensor hallucis tendon to the dorsum of the foot.

#### CONCLUSION

A satisfactory method for obtaining solid fixation of the interphalangeal joint of the great toe, as herein described, in our hands has materially improved the result in arthrodesing operations of the interphalangeal joint of the great toe. This method was used initially in those cases in which bony fusion had failed to occur but at the present time we are using it routinely on our service and are obtaining excellent results.

#### REFERENCE

TILSON, R. G. *J Bone Surg* 340, 1931.

# DUSTING POWDER GRANULOMAS FOLLOWING SURGERY

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IT has been occasionally observed (7) that talcum powder, hydrated magnesium silicate, used so extensively and often so carelessly as a glove and dusting powder is capable of producing granulomas in tissue.

Feinberg has reported granulomas in the subcutaneous tissues of patients who had previously had thyroidectomies. Antopol has observed the lesions in a group of patients in whom the granulomas were produced by lycopodium spores, following the use of this material as a dusting powder, and has reported 1 case produced by talc. Here the lesions were found in the serosa of the appendix.

Ramsey and Douglas (8) have recently reported the finding of talc granulomas in various localities and caution against the use of the material in abdominal surgery.

That talc produces a form of peritoneal inflammation is attested by McCormick and Ramsey (6), and that silica can give rise to granulomatous masses which may be mistaken clinically for neoplasms has been shown in a report of such a mass developing in the scar from a scalp laceration (5).

Occasionally the pathologist is called into the operating room to have the surgeon point out small peritoneal lesions, some just visible to the naked eye, some as large as 2 millimeters in diameter. These may be on the appendix, the oviducts, the peritoneum of the uterus, or the coils of the intestine. There may be but a single lesion or there may be many. There is no free fluid in the abdomen and adhesions may or may not be present. The surgeon invariably suggests tuberculosis or carcinomatosis.

The lesions are discrete. A small aggregation of them may give the appearance of coalescence. They are covered by an intact layer of peritoneum unless they may be located within some adhesions (Fig 1). There is no visible reaction of the surrounding tissues. The lesions escape notice in the ovaries (Fig 2) and the omentum because of the irregular surface of these structures. They are occasionally seen on the surface of the liver if the previous surgical interference has been in this region. Inquiry reveals that every one of these patients has had a previous laparotomy.

Routine histological sections of the lesions show tiny granulomas consisting of one or a few giant cells, surrounded by a few lymphocytes and macrophages and a mild proliferation of histiocytes which may have the appearance of epithelioid cells. Even histologically some of the lesions may resemble tubercles and that some have been mistaken for tuberculous lesions is understandable (Fig 3). Gardner has commented upon the similarity of tuberculous and silica lesions.

If the lesions are scrutinized carefully by the ordinary illumination, foreign body material may or may not be seen in them. But if polarized light be used, the silicate crystals will be seen to stand out in brilliant illumination as an electric sign in a night sky. Cellulose fibers from gauze and cotton behave in a similar manner (Fig 4). Both of these substances, chemically inert, are quite likely to be unseen in routine sections with the usual source of illumination.

So useful is polarized light that we have come to use it routinely in all granulomatous and cicatricial lesions.

It has been our observation that if interval or serial sections are routinely taken through the omentum of patients previously operated upon and these sections are studied with polarized light, granulomas and crystals will almost always be found. The large number of crystals found in the omentum is due to the natural scavenger activity of the cells of that structure. It might be added that fragments of cellulose fibers from surgical sponges are likewise occasionally found where they too induce a similar type of foreign body reaction.

The frequency with which these granulomas are found in the serosal layers of the viscera and in adhesions has led us to speculate upon the relation between dusting powder and adhesions.

Prompted by the constant association of talc granulomas and adhesions in patients previously operated upon, the following two sets of studies have been made: (1) An analysis of 50 hospital patients presenting talc granulomas in various localities, (2) a study of such lesions produced experimentally in laboratory animals.

## PATIENTS PRESENTING TALCUM GRANULOMAS

Fifty consecutive unselected hospital patients previously operated upon and presenting talcum

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Fig. 3. Routine illumination. Granuloma with crystals and giant cells in tubal adhesions.



Fig. 4. Polarized light. Granuloma with crystals in cortex of ovary.

granulomas were subjected to careful study. The following points were noted in the study: (1) the patient's sex and age; (2) the symptoms for which the patient came to the hospital; (3) the date and type of present operation; (4) the number of previous operations; (5) the date and type of previous operations; (6) the presence, location, and amount of adhesions; (7) the macroscopic description of the surgical specimens; (8) the site of and an estimate of the number of talcum granulomas as shown by the histological sections which were made in each case.

The purpose of these studies was to correlate, if possible, the number of talcum granulomas, and therefore the volume of talcum, with the pathology seen in the abdomen and the amount of adhesions observed.

An analysis of the cases studied showed the following:

1. Sex and age had no bearing upon the pathology.
2. Every case had had previous surgical operation of some type.
3. Of the 50 patients studied 42 had had 1 pre-

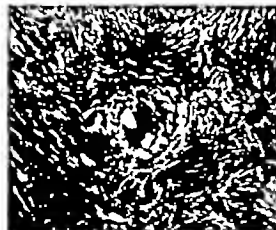


Fig. 5. Polarized light. Small granuloma in cortex of ovary with giant cell containing large crystal. With ordinary illumination the lesion resembles young tubercle.

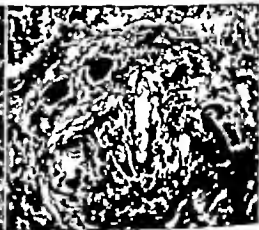


Fig. 6. Granuloma in appendiceal scar. By polarized light, this section is found to contain both cellulose fibers and talc crystals.

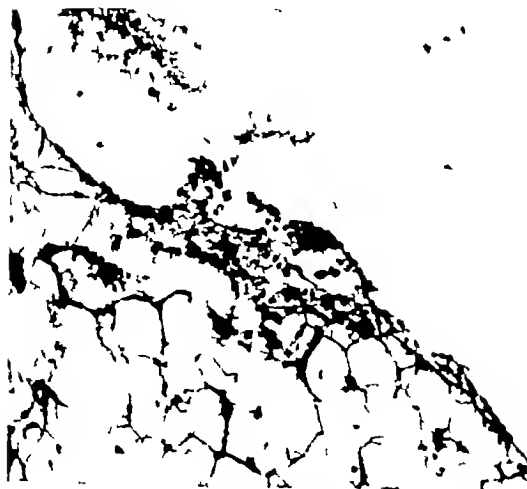


Fig 5 Routine illumination Talc crystals on contact with peritoneum are rapidly surrounded by proliferating serosal cells Guinea pig, 24 hours

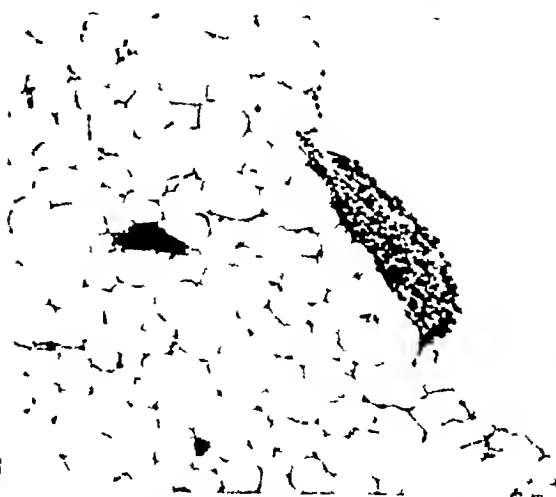


Fig 6 Routine illumination Talc crystals covered by an intact layer of serosal cells, forming young granuloma Guinea pig, 48 hours

vious operation, 7 had had 2 previous operations, and 1 patient had had 5 previous operations

4 The time interval between the operations was of no apparent importance

5 In so far as the information was available in the patients' records there was no apparent correlation between the symptoms and the talc. It was observed that some of the patients complained of the same symptoms for which they had originally sought relief

6 In general it was observed that adhesions were more abundant in patients who had had

more than 1 previous operation and that the more extensive the surgery the more abundant the adhesions

7 Of the 50 patients presented, 40 showed intra-abdominal granulomas

8 Forty-one patients were women, who are more often the victims of surgery than men (often useless surgery)

9 Every patient showing intra-abdominal granulomas also showed adhesions. There was a constant association between the presence of silicate and adhesions



Fig 7 Polarized light Talc crystals shown in young granuloma, covered by intact layer of serosal cells



Fig 8 Routine illumination Young granuloma sinks to plane of surrounding serosa





Fig. 9. Polarized Light. Young peritoneal granuloma containing crystals. It has sunk to plane of serosa and is covered by an intact layer of serosal cells.



Fig. 10. Polarized light. Peritoneal granuloma, i.e., containing giant cells, each contains the crystals. Lenses surrounded by fibroblasts.

10. Five patients submitted to surgery for no other reason than for liberation of adhesions.

11. Of the 50 patients, 10 presented granulomas in areas other than the abdomen: 6 cases of granulomas occurred in sinus tracts in which lesions failed to heal following previous surgery; 3 patients presented incisional tumor masses, 1 thought to be a neoplasm; 1 thought to be an incisional hernia (Fig. 4); another a cold abscess. Another patient developed granulomas in the cicatrix of a circumcision, and this necessitated further surgery for marked phimosis.

12. One patient who had previously had a caesarean section presented the interesting combination of dusting powder granulomas and of

proved tuberculous peritonitis and salpingitis, the tuberculous and the silicate granulomas coexisting in the same microscopic field.

13. Of the 40 cases presenting abdominal lesions, talc granulomas were found in the following sites: In the omentum, 20 times; in the ovary 18 times; in adhesions, 15 times; in tubes, 9 times; in wall of intestine, 5 times; in serosa, appendix, 1 time.

In order, if possible, to determine the quantitative relation between the amount of silicate used and the abundance of the adhesions, the sections and the notes dictated by the surgeon were studied, independently. When 3 granulomas or less per section were found the silicate was termed



Fig. 11. Polarized light. Granulomas with crystals and giant cells in cortex of the ovary.

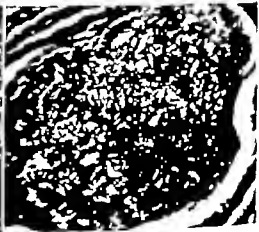


Fig. 12. Polarized Light. Granulomas with crystals and rabbit adhesions following transection of the serosa.



The first of these rabbits was sacrificed at the end of 3 hours. At autopsy the peritoneal cavity contained an estimated 3 cubic centimeters of definitely cloudy fluid, slightly yellow in color. About cubic centimeter as pipetted off into small tube and allowed to stand at room temperature. No coagulum formed at the end of hour. The abdomen showed no macroscopic evidence of inflammation. A few solitary ink-like flecks were attached to the peritoneal surface and these could not be wiped off. They are obvious aggregations of talc. Specimens from these areas were taken for histological examination.

The fluid removed by pipette was examined cytologically, supravital stain (Ehrlich's neutral red and Janus green) being used. The following cellular elements identified are listed in order: monocytes, large numbers, macrophages, numerous, lymphocytes, few serosal cells, occasional polymorphonuclears, occasional.

One or two macrophages contained some ink-like crystals. A few free crystals are seen but care must be exercised in recording free crystals in hospital here talc is so abundant in the air and upon glassware how ever scrupulous the technique.

Autopsy as done on the second rabbit at the end of 4 hours. The findings practically duplicated those in the first. The cellular response in the peritoneal fluid as essentially the same. All the talc had been immobilized and there was none free in the fluid. There were no adhesions.

The character of the cells found in the fluid, the almost complete absence of polymorphonuclears and the absence of fibrin bespeak the noninflammatory quality of the talc.

Histological examination of the peritoneal plaques found in these rabbits showed series of changes in the peritoneum which may be described briefly as follows: When the silica crystal makes contact with the serosal surface, the serosal cells in the immediate vicinity lose their flat appearance become globoid, and begin to proliferate. Very soon the crystal is seen lying in a cap composed of these cells. This cap-like mass is elevated above the surface of the serosa resembling normal serosa (Fig. 5).

The cap is rapidly closed across the top by proliferating serosal cells which completely cover the crystal (Fig. 6). As the process goes on there is proliferation of histiocytes in the deeper layers in the vicinity. A few monocytes and macrophages appear the beginning of granuloma. Very soon the young granuloma instead of projecting above the surface (Fig. 7) comes to occupy position in which there is little if any alteration of the serosal plane and lies definitely beneath the surface, covered by an intact, smooth layer of serosal cells (Fig. 8). The crystals now usually lie, especially if single in such a way that their long axes are parallel with the serosal surface.

During the process no exudate of fibrin is seen.

As the granuloma develops giant cells are seen and the crystals may be demonstrated thus the cytoplasm of these cells or lying in the interstices between epithelioid cells (Figs. 9, 10).

In some organs, especially the human ovary the granulomas may be seen at considerable distance, often as much as millimeter or more, beneath the surface (Fig. 11).

In the mechanism of the formation of adhesions it is well known that fibrin plays an important part. The inability of silica, *per se*, to induce an exudation of fibrin would suggest that it is not important in the formation of adhesions. These observations would point to a very efficient mechanism of disposal of talc by the peritoneum.

*Experiment 4. Laparotomy no incision, talc suspension.* Ten normal rabbits were selected. With aseptic technique under intra-venous anesthetic anesthesia reinforced by ether the abdominal cavity was entered through midline incision. Cubic centimeters of sterile 10 per cent talc suspension as introduced into the abdominal cavity. The contents of the cavity were left unattended and the incision was closed with 10 layers of sutures.

At the end of 4 weeks autopsy as performed upon the rabbits. The incisions were all healed. About evidence of infection. One rabbit showed some adhesions between the large intestine and the anterior abdominal wall at the site of the incision. Another rabbit showed only generalized adhesions. A few minute, yellowish granulomas were seen in the peritoneum and in the omentum.

Histological examination showed typical talc granuloma, covered by an intact layer of serosal cells.

For control purposes under aseptic technique and with intra-venous anesthetic anesthesia reinforced by ether the abdomen of third rabbit was opened and 10 cubic centimeters of sterile physiological saline as introduced into the abdominal cavity. The abdomen was closed with 10 layers of sutures. At autopsy at the end of 4 weeks this rabbit showed no generalized adhesions, and there was no evidence of any abnormality of the organs or the peritoneum.

*Experiment 5. Laparotomy no incision, dry talc.* Under aseptic technique and with intra-venous anesthetic anesthesia supplemented with ether the abdomens of rabbits were opened through midline incision.

Without disturbing the contents of the abdomen were sterile dry talc as dusted on the coils of the intestine. The abdomens were closed with 10 layers of sutures.

The rabbits were examined post mortem at the end of 4 weeks. A small pyogenic abscess as found in the lower end of the incision in one of the rabbits. The lay external to the peritoneum and had no communication with the peritoneal cavity. There are no generalized adhesions in either rabbit. Numerous yellowish granulomas are found in the peritoneum of the large intestine, the omentum, and in the flanks in the region of the extremities of the oviducts and ovaries. The granulomas are larger than those found in the animals of experiment 4. This probably could be accounted for by both the uneven distribution of the powder its adherence to moist surfaces, and its consequent slower dissemination throughout the abdominal cavity.

Histologically the granulomas are larger and contain great masses of crystals. The lesions as usual are covered by an intact layer of serosal cells. Adhesions of the kind without exudate. No other control animals were used in this experiment.

*Experiment 6. Laparotomy oophorectomy incision, talc and talc suspension.* With aseptic technique and under intra-venous anesthetic anesthesia reinforced by ether the abdomens of rabbits were opened through midline incision. A unilateral oophorectomy was done on both rabbits and the peritoneum of the small intestine of each was vigorously rubbed with sterile dry gauze, to translocate especially the serosa. In addition, the serosa was repeatedly scarified with the scalpel. One hundred cubic centimeters of 10 per cent sterile talc suspension as introduced into the peritoneal cavity of one rabbit and the abdomen was closed with 10 layers of sutures.

For control purposes the abdomen of the other rabbit was closed without the addition of the talc suspension. Autopsy on both rabbits as performed at the end of 4 weeks. Both rabbits showed adhesions between the small intestine and the anterior abdominal wall at the site of the incision. So far as could be determined macroscopically the adhesions are no more abundant in the talc treated





This small work is truly one that arouses enthusiasm. There is not a line that does not express some salient fact. It reads like an engrossing story and the illustrations are most instructive. The surgical profession owes a debt of gratitude to the author for this excellent monograph.

JOHN A. WOLFER

CLINICIANS, both internists and surgeons, will welcome the volume on gastric carcinoma by Walters, Gray, Priestley, and their associates of the Mayo Clinic.<sup>1</sup> Backed as it is by a tremendous experience in gastric surgery, it lays particular stress on methods of diagnosis of small and early malignant lesions. A historical introduction is followed by chapters on diagnosis, roentgenology, gastroscopy, special laboratory observations, physiological considerations, indications for treatment, pathological considerations, preoperative treatment, anesthesia, a detailed discussion of the various technical procedures, prognosis, end-results, and statistical data.

Rightfully so, considerable space is devoted to the diagnosis of early lesions and other differential diagnoses of doubtful lesions in chapters on x-ray, gastroscopy, and clinical diagnosis. Emphasis is laid on the need for early exploration in doubtful lesions that do not promptly respond to medical management and stay healed. Chapters on surgical treatment are written with close attention to technical detail and are excellently and profusely illustrated, as is the text throughout.

While the written text is the product of some fifteen or twenty men, it is all interestingly written and makes good reading. This volume is a complete and up-to-date survey of gastric cancer.

J. R. BUCHBINDER

THE English author, Bramwell from Manchester, and the American, King from Johns Hopkins, state in the preface to their *The Principles and Practice of Cardiology*<sup>2</sup> that the purpose of their text is to present two views, "clinical observation" as the fundamental viewpoint of the British, and "laboratory methods" as the predominant American issue. They also indicate that the volumes are "impregnated by a strongly personal flavor." On this basis, Dr. Bramwell presents his ideas in the first 238 pages, and Dr. King writes the latter half.

History, physical examination, cardiac pain, heart sounds, are discussed by Dr. Bramwell in the conventional manner. There is a chapter on heart disease and pregnancy and also an interesting chapter on "athlete's heart." His discussion of the pulse and cardiac arrhythmias contain the diagrams, sphygmograms, and electrocardiograms of the current Eng-

lish textbooks, as well as phonocardiograms. The reader may question whether these are English "clinical observations" or laboratory methods.

Dr. King presents the American viewpoint in the manner recommended by the American Heart Association from an etiological aspect, covering the distribution, and the various types of heart disease: congenital, rheumatic, bacterial, syphilitic, hypertensive, and others. He devotes a special chapter to the "senescent heart" which is a somewhat indefinite term, contrary to American idea. In general, his precepts are thoroughly conventional.

The book, or better the two volumes in one book, presents the ideas of a British and an American author. If adverse criticism were to be offered, one might contend that an attempt was made to cover too much material in too few pages, in the ordinary textbook fashion.

CHAUNCEY C. MAHER

IN the second edition of Dr. Wangenstein's outstanding monograph<sup>3</sup> he has enlarged particularly upon diagnosis and treatment, indications for, and technique of, surgical procedures, many illustrations have been added.

The particular points of value, which make this volume a "must" to all students of surgery are its adherence to sound physiological principles, its detailed devotion to pathology, to the diagnosis and recognition of types and locations of obstructions, and above all, the clear recognition of the place and indication for both conservative and operative attack. The author has compiled a voluminous bibliography. His illustrations and photographs of apparatus and surgical technique leave nothing to be desired in this phase of his work.

In part 1 is a lucid and physiologically sound discussion of the sources and effects of distention locally and systemically, of absorption in obstruction, and also of the pathology of strangulation. Part 2 is a detailed discussion of the diagnosis of acute abdominal lesions, methods of recognition of the presence of obstruction, and the differential diagnosis of simple and strangulating obstruction. Part 3 covers treatment and embodies an extensive and detailed description of conservative methods of decompression and operative procedures. There is a comprehensive discussion complete with illustrations, of standardized bowel operations, including a chapter on closed aseptic resection. Part 4 covers the special obstructions, such as obstructions of congenital origin, foreign bodies, volvulus intussusception, and the like.

The reviewer has had the privilege of expressing his opinion in a review of the first edition of this work. He has carefully read the second. In his candid opinion few monographs in modern surgical literature represent the standard of excellence as set forth in this volume on bowel obstruction.

J. R. BUCHBINDER

<sup>1</sup>CARCINOMA AND OTHER MALIGNANT LESIONS OF THE STOMACH By William Walters, B.S., M.D., M.S. in Surgery, D.Sc., F.A.C.S., Howard K. Gray, B.S., M.D., M.S. in Surgery, F.A.C.S., and James T. Priestley, B.A., M.D., M.S. in Experimental Surgery, Ph.D. in Surgery, F.A.C.S., Philadelphia and London: W. B. Saunders Co., 1942.

<sup>2</sup>THE PRINCIPLES AND PRACTICE OF CARDIOLOGY. By Crighton Bramwell, M.A. (Camb.) M.D. (Manch.) F.R.C.P. (Lond.), and John T. King, A.B., Princeton, M.D., Johns Hopkins. F.A.C.R. London: Humphrey Milford (Oxford University Press) 1942.

<sup>3</sup>INTESTINAL OBSTRUCTION: A PHYSIOLOGICAL AND CLINICAL CONSIDERATION WITH EMPHASIS ON THERAPY INCLUDING DESCRIPTION OF OPERATIVE PROCEDURES. By Owen H. Wangenstein, B.A., M.D., Ph.D. 2d ed. Springfield Ill. and Baltimore Md.: Charles C. Thomas 1942.

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

**A TEXTBOOK OF G. NEUROLOGICAL SCIENCE.** By Sir COWLEY Berkeley M.A. M.C., M.D. Cantab. F.R.C.P. Lond. F.R.C.S. Lond. M.M.S.A. (Hon.), F.R.C.O.G., and Victor Bonney M.B. M.D., B.Sc. Lond., F.R.C.S. Edg. F.R.A.C.S. M.R.C.P. Lond. 4th ed. London, New York, Toronto and Melbourne: Cassell & Co. Ltd., 1942.

**THE ANTROPOLOGICAL FACTORY: WITH CONSIDERATION OF THE ANTHROPOMY PROBLEM.** By Bernard Zondek and Felix Sulzhan. Baltimore: The Williams & Wilkins Co., 1942.

**MANUAL OF GYNECOLOGICAL THERAPY INCLUDING CARBON DIOXIDE, HELIUM, AND WATER VAPOR.** By Albert H. Andrews, J. M.D. Chicago: The Year Book Publishers, Inc., 1942.

**HEALTHY BABIES ARE HAPPY BABIES; A COMPLETE HANDBOOK FOR MODERN MOTHERS.** By Josephine Hoenigway Kenyon, M.D. 2d ed. Boston: Little, Brown & Co., 1942.

**PSYCHOSOMATIC MEDICINE: THE CLINICAL APPLICATION OF PSYCHOLOGY TO GENERAL MEDICAL PROBLEMS.** By Edward Weiss, M.D. and O. Spurgeon English, M.D. Philadelphia and London: W. B. Saunders Co., 1942.

**INDURATION, ITS DIAGNOSIS AND MANAGEMENT: WITH SPECIAL REFERENCE TO DYST.** By Martin E. Robins, M.D. Philadelphia and London: W. B. Saunders Co., 1942.

**ORTHOPEDIC SUBJECTS.** Prepared and edited by the Subcommittee on Orthopedic Surgery of the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Philadelphia and London: W. B. Saunders Co., 1942.

**ATLAS OF OVARIAN TUMORS.** By Gertner Benfald, M.D. 1th. Preface by Fred W. Stewart, M.D. New York: Grune & Stratton, 1942.

**TRANSACTIONS OF THE SIXTY-THIRD MEETING OF THE AMERICAN SURGICAL ASSOCIATION.** Edited by Walter Estell Lee, M.D. Vol. 66. Philadelphia: J. B. Lippincott Co., 1942.

**TREATMENT OF FRACTURES.** By Guy A. Caldwell, M.D. F.A.C.S. New York and London: Paul B. Hoeber Inc., 1942.

**REPORT OF THE CLINICAL CANCER RESEARCH COMMITTEE OF THE BRITISH EMPIRE CANCER CAMPAIGN.** Reprinted from the British Empire Cancer Campaign, 1942.

**THE EIGHT SA. 12.** By C. J. Gerling. New York: The House, 1942.

**ENDOSCOPIC TREATMENT OF THE STOMACH.** By ROBERT W. KERR, M.S., M.D. F.A.C.S. St. Louis: The C. V. Mosby Co., 1942.

**FRACTURES OF THE JAW AND OTHER FACIAL BONES.** By Glenn Major, B.S. A.M. (Path.), M.S. (Expt. Surg.) Ph.D. (Surg.), D.D.S. M.D. F.A.C.S. 1st chapter on Radiographic Technique by Lester M. J. Freedman, B.S., M.D., and War Aspects of Jaw Fractures by Arthur Doherty, D.D.S., M.D. St. Louis: The C. V. Mosby Co., 1942.

**BRONCHITIS, PNEUMONIA, PNEUMOTHORAX AND TUBERCULOSIS.** By JAMES R. LAW, B.S. M.D. and MILES B. ROSENBLATT, M.S. M.D. London, New York, Toronto: Oxford University Press, 1942.

**PANCREATIC FUNCTION AND PANCREATIC DYSFUNCTION: STUDIED BY MEANS OF SECRETIN.** By HENRIK O. LARSEN, M.D. Translated by Helen D. Fry. 1th. Foreword by Joseph H. Pratt, M.D. New York: The Macmillan Co., 1942.

**REMOVAL AND GRAFT FOR EXTRA-ARTICULAR SPONTANEOUS WITH SPECIAL REFERENCE TO ANTEROCEDRAL HYPERCALCAEMIA.** By NATHAN R. JAMES, L.R.C.P. & S. (Ed.), D.I. (R.C.P. & S. Eng.). London: J. & A. Churchill, Ltd., 1942.

**RENAL LITHIASIS.** By Charles C. Higgins, M.D. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1942.

**A SCROLOTT'S FRONT TO RECENTLY METASTASIZING TUBERCULOSIS.** By Fred H. Allen, M.D. F.A.C.S., F.I.C.S. 1th. Foreword by Lowell Thomas. New York: E. P. Dutton & Co., Inc., 1942.

**PORTALS AND VISCERA.** By JESSIE L. STOVERSON, R.N. New York: Joint Orthopedic Nursing Advisory Service of the National Organization for Public Health Nursing and the National League for Nursing Education, 1942.

**ORTHOPEDIC CONDITIONS: 2. BONE-SETTING KNOWLEDGE.** By JESSIE L. STOVERSON, R.N. New York: Joint Orthopedic Nursing Advisory Service of the National Organization for Public Health Nursing and the National League of Nursing Education, 1942.

**ORTHOPEDIC NURSING: CONTENT AND METHOD OF THE TRAINING PROGRAM IN SCHOOLS OF NURSING.** By Catherine Calderwood, R.N. New York: Joint Orthopedic Nursing Advisory Service of the National Organization for Public Health Nursing and the National League of Nursing Education, 1942.

**CLINICAL PEDIATRICS.** By I. Newton Kugelmann, M.D., Ph.D., Sc.D. London, New York, and Toronto: Oxford University Press, 1942.

# SURGERY

## GYNECOLOGY AND OBSTETRICS

*An International Magazine, Published Monthly*

VOLUME 76

MAY, 1943

NUMBER 5

### INTUBATED URETEROTOMY

#### A New Operation for Ureteral and Ureteropelvic Stricture

DAVID M. DAVIS, M.D., Philadelphia, Pennsylvania

THE surgery of the ureter has lagged behind the surgery of the kidney in a manner that is difficult, now, to explain. Only a few years ago there was a general feeling that the ureter seldom required attention, except for the occasional case in which it had to be removed. This belief perhaps arose from the fact that, after pyelography was invented, the medium was always injected through a catheter lying in the renal pelvis. Pyelography brought about a rapid increase in our knowledge concerning renal pathology, much of it concerning the effects of obstruction. In conservative kidney surgery, attention centered upon plastic operations on the pelvis, with the result that the consideration, which now seems obvious, namely, that the cause of the pelvic dilatation must be an obstruction lying at some point in the ureter, was ignored. Next, ureteropelvic obstructions were treated by means of plastic operations, and much argument arose as to the desirability of using a tube splint after such operations.

Hunner's persistent campaign brought the realization that there are many ureteral obstructions below the ureteropelvic junction, and that many of these are amenable to treatment by dilatation. The operative treatment of strictures not responding to dilatation has

remained unsatisfactory, in fact, it is seldom attempted.

About 10 years ago, when faced with a dense, fibrous, thick walled stricture of the upper ureter, I applied the principle of the Rammstedt operation for pyloric stenosis, and divided the stricture longitudinally, passing through all the layers of the ureteral wall except the mucosa (Fig. 1). The result was most satisfactory. Good results have since been obtained with this technique by Bidgood and Roberts, Gibson and others, and the operation is now generally adopted for the comparatively few cases in which the method is applicable.

The question of splinting after ureteropelvic plastic operations came up every time such an operation had to be done. Opinions have varied radically as to the value of the splint. Peck, Harris, Cabot, Moore, Sargent, Priestley, and Ormond have all favored splinting. Gibson puts the case for splinting as follows: "No matter how generous the surgeon is in the use of sutures in plastic repair, the outcome is likely to be a failure unless he makes use of splinting, conversely, if he places his dependence on adequate splinting the result will almost certainly be successful even though he uses no sutures at all." In spite of this, Gibson states that he does not "eschew the use of sutures entirely."

From the Department of Urology, Jefferson Medical College.



In quoting authorities for the use of the ureteral splint it should not be forgotten that Albarran recommended that whenever the kidney is opened as large a ureteral catheter as possible should be passed down the ureter and left in place for several days.

It seemed to me that the results were better in the splinted cases, but splint or no splint, there were all too many failures, partial or complete.

Another aspect of the problem appeared as the result of experiences with urethral strictures. I had occasion nearly 20 years ago to operate upon a patient with a very severe bulbomembranous stricture accompanied by extensive perineal scarring and multiple fistulous tracts. After the scarred, diseased tissue was laboriously dissected away there was left a huge hole in the perineum, and a narrow ribbon of urethral wall representing a part of the roof of that organ bridging a gap in the urethra a good inch and a quarter long. I lacked the courage to extend the dissection far enough to permit the freeing of the urethra, freshening of its ends, and circular suture in the classic manner. Instead, I passed a No. 24 F catheter through the entire length of the urethra into the bladder, fastened it in place and left the wound unsutured. The catheter was visible at the bottom of the cavity for many days but after 2 weeks it was covered by healthy granulations. At the end of 3 weeks it was withdrawn, and the result was so excellent that no later dilatations were required. Evidently the epithelium had grown around the circumference of the catheter and a new urethra, healthy and pliable was created. Welland Howard has since described a similar procedure in which if necessary he even splits the urethra into several ribbons to permit the passage of the catheter.

In June, 1930 I was confronted by a narrow thin-walled stricture of the upper ureter just at the point where the ureter disappeared into a kidney with a completely intrarenal pelvis (Fig. 2 a). The absence of an extra renal pelvis removed any possibility of using any of the usual plastic operation. The Rammstedt type of operation was out of the question, as the wall of the ureter at the site of the stricture seemed even thinner than the

wall of the normal portion of the ureter. As I was to know what to do I finally decided to apply the same principle used so successfully in urethral strictures, that is, to introduce a tube splint which was to remain in place for 2 or 3 weeks. A description of this case follows.

**CASE 1.** M. D. B. aged 6 years. I was called to see this patient because of attacks of mictiduria, slowness and rheumatic fever. This patient had usually enjoyed good health. In March, 1930 there was an attack of pain in the right kidney region. This pain recurred fairly frequently, often accompanied by hematuria. There was no frequency.

Röntgenograms taken June 1, 1930, showed a small stone in the lower calyx of the right kidney and persistent narrowing of the uppermost part of the right ureter (Fig. 3, ). On June 2, 1930, No. 24 F bulb passed to the right kidney meeting moderate resistance. After this 1 or three more attacks of pain, with hematuria occurred, and roentgenograms showed the stone to be in the pelvis proper. It was felt that the narrowing seen in the roentgenogram must represent an obstruction, otherwise this small stone could have become engaged in the ureter.

Operation as performed August 2, 1930. The kidney easily exposed and freed. The ureter brought down on tape. The upper portion of it was markedly adherent and dissected in discrete and firm fibrous capsule. Splint inserted with this thin found perfect ureter. The pelvis was entirely intrarenal with only a very slight indenting at the hilum. The main artery entered the hilum around the side of the ureter. About 5 cm. below the kidney there was a sharp narrowing of the ureter evidently congenital. The wall was no thicker than normal and there was no evidence of any inflammatory change in the wall. A small artery joined the ureter at this point. It could be ligated and divided. A considerable portion of the fibrous capsule was cut. Ureterotomy was made by the upper part of the kidney but the hilum could not even be felt. Probes and forceps of all kinds were used to explore the kidney but the stone could not be located. A roentgenogram made on the table and nephrotomy made over the shadow as nearly as could be made out. In spite of this, the stone could not be found, and further effort was abandoned in order to avoid damage to the kidney. The retrolateral incision extended down through the structure. A Rammstedt operation could not be done as the ureteral wall was everywhere of normal thickness. A rubber catheter brought down through the nephrotomy into the ureter. The ureter as closed with a suture. A defect remained in the part of the ureter (Fig. 4 d). It was decided to leave the tube in place at least 2 weeks in the hope that the ureter could grow around it thus relieving the stricture.

and making it possible for the stone to pass should it again become free in the pelvis

There was some wound infection, with fever. The tube was removed on the 14th day, and 48 hours later all urinary drainage had ceased. He left the hospital on the 27th day.

On October 17, 1940, the patient felt very well and had had no more attacks. The urine contained a few pus cells and some staphylococci. On October 24, 1940, intravenous urogram showed a small stone shadow, apparently in a calyx or in the parenchyma. The upper ureter was well shown and was uniform in diameter, the persistent narrowing formerly seen being entirely obliterated (Fig 3 b). On August 23, 1942, the patient reported by letter that he was in perfect health, engaging in very heavy physical labor, as well as in active social life, and had never had the slightest recurrence of pain in the kidney.

The excellent result obtained encouraged me to follow the same plan in another similar case.

**CASE 2** Mrs A K, aged 46 years. Pain in the left kidney began in 1917. Calculous pyonephrosis was found in 1925, and the left kidney was removed. For one year before admission, there were occasional pain in the right back, slight burning on urination, dizziness, and nervousness, but no frequency of urination. There was pyuria, and x-ray examination showed a stone shadow in the right kidney region.

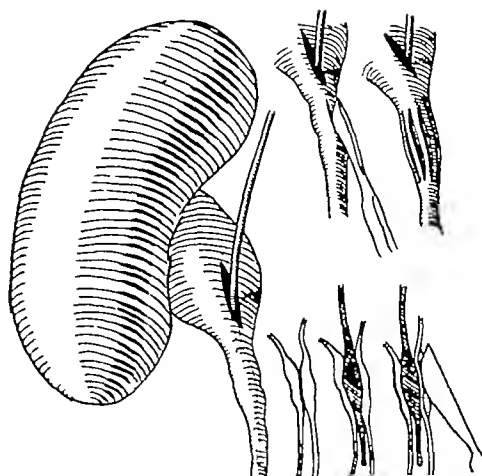


Fig 1 Rammstedt type operation for thick-walled ureteral stricture. The stricture is stretched by a bougie inserted through a pyelotomy incision, one or more longitudinal incisions are made passing through all layers of the ureteral wall except the mucosa.

The urine contained many bacilli. Phenolsulfonphthalein test returned 18 per cent in one-half hour. Pvelography showed an abnormal, irregular, but not particularly dilated pelvis in a large kidney shadow, and a normal ureter. The stone extended to the ureteropelvic junction.

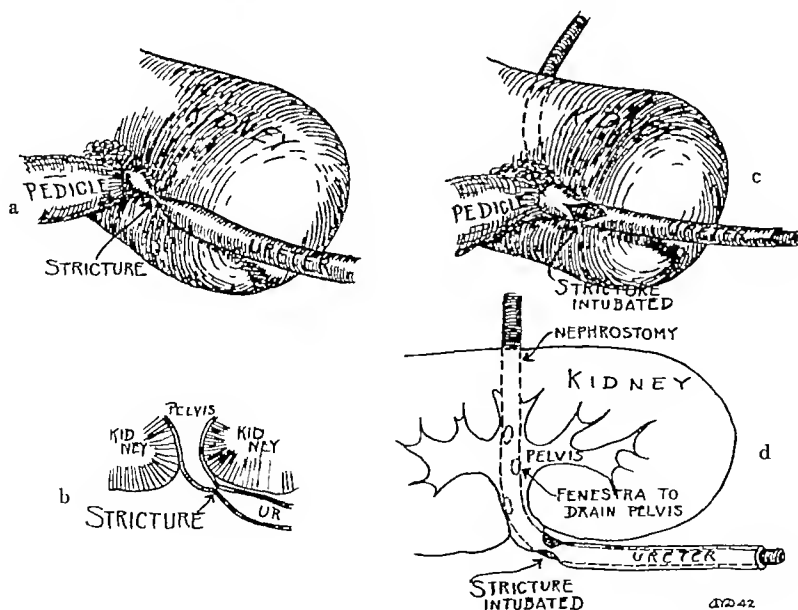


Fig 2 Case 1. a, Conditions as found at operation, b, diagrammatic section through ureter as it entered kidney, c, stricture incised, splint tube in place in ureter, proximal end brought out through nephrostomy incision, d, diagrammatic section showing conditions at end of operation.

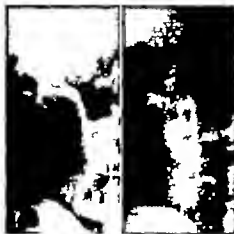


Fig. 3. Case 2, left. Intra-eneous pyelogram, before operation, showing stricture of upper ureter. b. Intra-eneous pyelogram, 3 months after operation, showing stricture no longer present.

On May 21, 1931, operation as performed. The upper ureter was cocooned in thick mass of indurated fat. The pelvis was entirely intrarenal, but the stone fortunately could be removed through a long ureterotomy. The ureter was definitely narrowed below the kidney. A rubber tube about No. 4 F in size, and equipped with many fenestrae, was passed down the ureter a few centimeters, and brought out through small nephrotomy incision (same as Case 1). Retrol sutures were used and the tube was exposed in the open retroperitoneum.

The tube was accidentally pulled out on the 10th postoperative day and there was practically no urinary drainage afterward. The wound healed *per primam*. The patient was out of bed on the 4th day and left the hospital on the 8th day.

A month later 36 per cent phenolphthalein was excreted in one-half hour and the patient felt perfectly well. Two months later the ureter was dilated with a No. 4 F bulb. The urine was clear and contained no pus, blood, or bacteria. Later the ureter was dilated twice to sizes No. 6 F and No. 4 F. On July 1931 the patient felt perfectly well, and the urine was clear and uninfected. A postoperative pyelogram has been taken.

Not long afterward a third case presented itself. The situation differed somewhat in that there was a good-sized extrarenal pelvis, and the stricture was considerably longer.

CASE 3. Mrs. B. F., aged 35 years. This patient had been troubled with marked pain in her right side since the birth of her first child. Investigations in the hospital showed that the left kidney and ureter were normal, the right kidney pelvis moderately but definitely dilated with persistent

marked narrowing just below the ureteropelvic junction, suggesting an aberrant blood vessel. The ureter below this point was also slightly dilated, suggesting another slight stricture at the lower end (Fig. 4).

Operation as performed November 19, 1931. The external appearance of the kidney was perfectly normal and it was not adherent, and as freed by dissection. The ureter below the kidney appeared perfectly normal. It was brought up on a bayonet dissection and then carried upward, thus disclosing a marked stenotic area about 1 centimeter in length just below the ureteropelvic junction. There was an aberrant artery above this point, the extrarenal pelvis was markedly distended even when the ureter below was quite empty (Fig. 5). All of the intrarenal tissue and blood vessels were dissected away from the stenotic area very carefully. It was found that there were coils of fibrous tissue completely surrounding the pelvis, and these were divided and stripped away. Pyelotomy was then made, and the urine spouted out under considerable pressure. The edges of this incision were held up with fine black silk traction sutures. A No. 14 bulb could just be forced through the area of stenosis, disclosing the fact that its walls were very thin, even thinner than those of the normal portion of the ureter. A No. 14 bulb could not be passed through the stricture. With the No. 14 bulb held in place, the ureter was incised longitudinally until the bulb passed freely down into the lower ureter. A small rubber tube about size No. 4 F was then prepared by cutting the end obliquely and it was passed down through the pyelotomy into the ureter about 33 centimeters below the incision in the ureter. A considerable area of this tube as exposed at the site of the incision. Three fenestrae were then cut in this tube so that they could lie in the pelvis. The pyelotomy was drawn together over the tube with suture of No. 000 plain catgut, but no sutures were used in the retroperitoneum (Fig. 3, b, c). The tube was brought out through the upper angle of the incision. The kidney, such as moderately movable, was fastened up to the muscles around the pelvis with one capsular suture of No. 000 chromic catgut. The ureter as then seen to be straight in a normal position.

The patient did very well. The incision healed *per primam* around the tube. The tube remained in place 5 days, draining considerable quantities of urine. On the 5th day it was clamped and removed, clamped for 24 hours with no leakage about it. There was very slight discomfort at first but this quickly disappeared. On the 5th day under the fluoroscope 10 per cent sodium solution was injected through the tube. It filled the pelvis quickly, outlined the ureter below the pelvis, and entered the bladder. A film was exposed. The tube was then withdrawn under observation by the fluoroscope. One could easily see the upper ureter and it had at least the same diameter as that below. The lower end was immediately exposed. Following the removal of

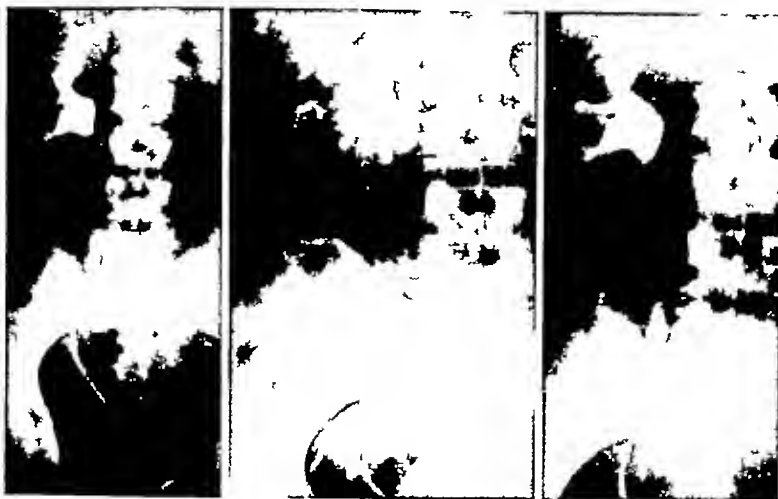


Fig 4

Fig 6

Fig 7

Fig 4 Case 3 Retrograde pyeloureterogram, before operation, showing marked ureteropelvic stricture

Fig 6 Case 3 Film made immediately after withdrawing tube. Arrow points to ureteral shadow of wide diameter at site of former stricture

Fig 7 Case 3 Retrograde pyeloureterogram 6 months after operation, stricture no longer present

the tube, no urine leaked through the incision, and the patient had no discomfort

Study of the x-ray films showed that immediately after the removal of the tube, the part of the ureter formerly strictured was very well outlined and retained the diameter of the tube at all points (Fig 6)

The patient's pain was entirely relieved. The urine remained clear and uninfected. The lower ureter was dilated on several occasions. On May 18, 1942, the retrograde pyeloureterogram shown in Figure 7 was taken, proving that the ureteral stenosis had been completely eliminated. At present the patient is perfectly well.

In the fourth case an upper ureteral stricture was complicated by a membranous valve at the ureteropelvic junction. The operative method was now employed with great confidence as to the outcome.

**CASE 4** Mrs G I, aged 23 years. This patient had always been underweight, but enjoyed fairly good health until her first child was born 2½ years ago. She then developed what was diagnosed as postpartum pyelitis, which persisted. Symptoms of frequency and burning recurred from time to time, and there was usually a slight afternoon fever. She was examined by Dr George M Laws. The infecting organism was *Escherichia coli communis*. Indigocarmine appeared in 8 minutes from the right kidney, and did not appear in 15 minutes from the right. Retrograde pyelograms showed no evidence of obstruction on the right side, but a moderate hydronephrosis on the left, with an essentially normal

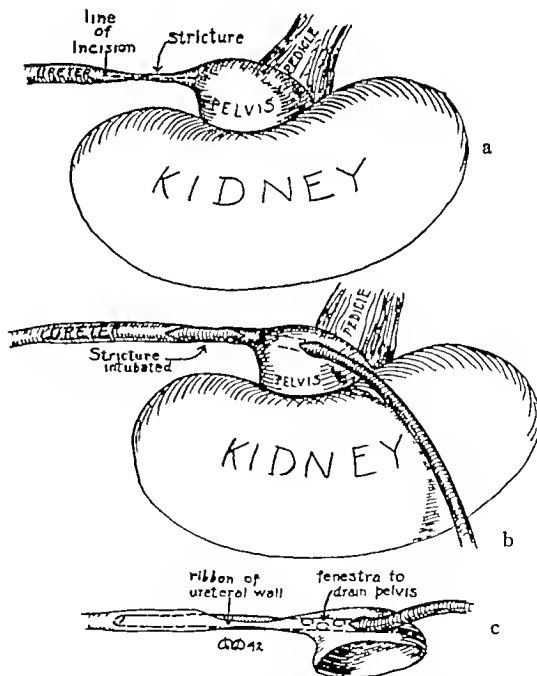


Fig 5 Case 3 a, Conditions as found at operation. The stricture is actually a little below the ureteropelvic junction, b, stricture incised, splint tube in place, proximal end brought out through pyelotomy incision, c, diagrammatic representation of conditions at end of operation

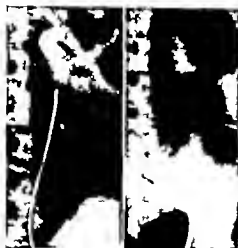


Fig. 8. Case 4. a, left, Retrograde pyelogram, before operation, the catheter partly lithiated, showing normal ureter and ureteropelvic narrowing. b, Intra-venous urograms, before operation. Film taken 1 hour and 45 minutes, showing retention in pelvis.

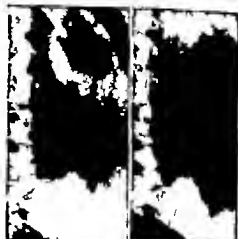


Fig. 9. Case 4. a, left, Intra-venous urogram, 36 months after operation. Film made at 3 minutes, showing excellent filling of pelvis. b, In the film made 1 hour the pelvis is shown to be practically empty.

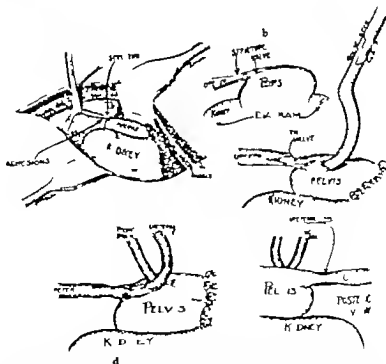


Fig. 10. Case 4. a, Conditions as found at operation. b, Diagrammatic section of ureter and pelvis, showing structure and valve. c, A/V pushed down in ureter by tip of clamp. d, Structure incised, A/V recovered, splint tube in place with proximal end brought on through pyelotomy incision, separate drainage. b, c, in pelvis. e, post-operative view—end of operation, showing ribbon of ureteral wall along splint tube.



Fig 11



Fig 13



Fig 14

Fig 11 Case 5 Retrograde pyeloureterogram, before operation, showing left hydronephrosis, ureter narrow and thread like in its upper third, lower two-thirds normal. Note large stones in right kidney.

Fig 13 Case 5 Pyelogram made by injecting through tube. Note outlines of new formed ureter alongside tube.

Fig 14 Case 5 Intravenous urogram made 6 months after operation. Note widely patent ureter, compare with Figure 11.

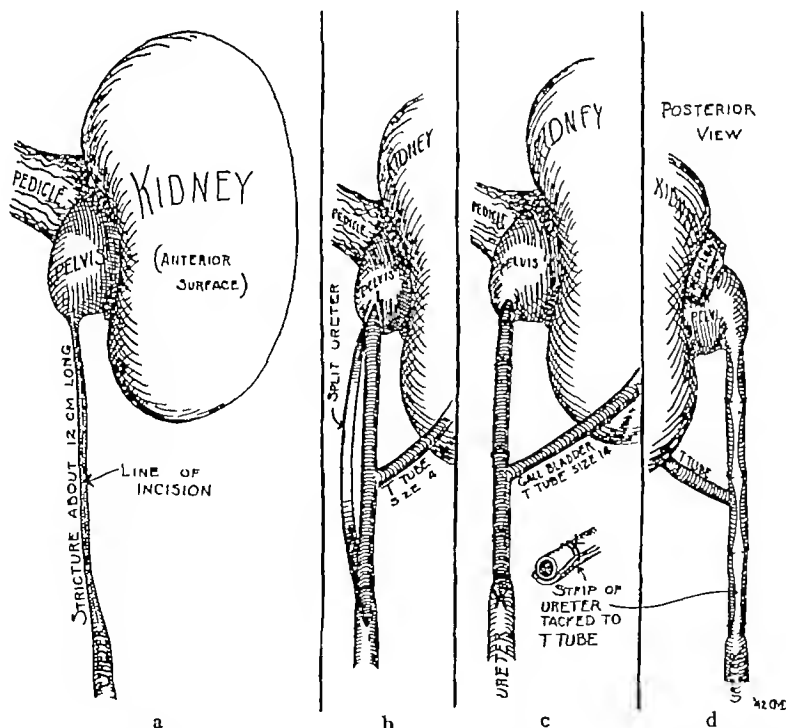


Fig 12 Case 5 a, Conditions as found at operation, b, stricture incised through its entire length, T tube in place. Note that ureteral ribbon does not stay in contact with tube, c, ureteral ribbon held to T tube by sutures, d, posterior view, showing ureteral ribbon closely applied to T tube. Stem of T-tube provides urinary drainage.



Fig. 3. Case of Dr. Edward L. Keyes. Intra-coccus urogram made 3 years after operation. Not likely patent upper ureter.

ureter suggesting retroperitoneal obstruction (Fig. 8, ) Intravenous urography showed similar picture with the right pelvis empty after 30 minutes, the left pelvis appearing later than the right and still well filled 1 hour and 45 minutes (Fig. 8, b). Treatment with sulfonamides brought about only temporary clearing of the line. The slight fever was so persistent that the patient feared she had tuberculosis and consulted Dr. B. Regis Gordon. I saw her November 4, 1931 at the request of Dr. Gordon and Dr. Lewis B. Scheffey. Dr. La. very courteously made his records and x-ray films available. On November 8, 1931 cystoscopy showed the bladder, ureteral orifices, and urethra normal. Line from the right kidney showed no pus or bacteria, that from the left side moderate number of pus cells and numerous clumps of bacilli. Phenol sulfonphthalein test. Appearance time right 4 minutes, left 4.5 minutes; collection time minutes; right 4 per cent, left 4.5 per cent transvesical trace. It felt that the condition of the left kidney was sure to grow progressively worse and operation, with the view of relieving the obstruction and saving the kidney, was advised.

Operation was performed December 6, 1931. The lower pole of the kidney was easily freed. The ureter was then brought upon tape and seemed to have normal position. Dissection was then carried carefully to the ureter. There was small clot in the perireteral fat running to the renal capsule in the lower pole but this was entirely a capsular vessel and there was no artery accompanying it. It was ligated and divided with no effect on the kidney. It was then possible to expose the pelvis very completely about exposing the upper half of the kidney just below the retroperitoneal junction the

ureter narrowed to less than half its diameter elsewhere. There are bands of fibrous tissue in the part of the ureter in the pelvis and the lower part of the pelvis as rounded and projected little below the ureteropelvic junction (Fig. 9, a, b). A small pyelotomy was then made and a grooved clamp inserted. I split of extension probing, it would not enter the ureter but all ways pushed out the lower portion of the pelvis. The ureter then reached, beginning at the point where the anastomosis began. The incision was carried upward and it could see within the ureter the tip of the grooved clamp covered by thin membrane evidently genital valve (Fig. 9, c). This was seized with forceps and excised with scissors. The clamp then passed freely down into the ureter. The incision was carried up a little way on the pelvis to expose a wide open ureteropelvic junction. A rubber tube of size N 14 F not fenestrated, was then passed through the pyelotomy down the ureter to a distance of about 3 centimeters below the ureterotomy. At the site of the ureterotomy the ureteral all now covered only about one-third of the circumference of the tube. N sutures were used. A No. 8 rubber catheter with the end cut off was then passed through the pyelotomy to drain the pelvis (Fig. 9, d, e). The kidney was replaced in position and the tubes were arranged so that the ureter followed normal course.

The convalescence was excellent and the incision healed *per primam*. On the 4th day there was transitory episode of fever. On the 16th day a catheter was inserted through the ureteral tube and immediately appeared in the bladder. The tube was then withdrawn. A short time later metacresol was injected through the pelvic tube and it was withdrawn. The next passage of urine was highly colored with metacresol. There was never any leakage of urine through the drainage tract. The patient left the hospital on the 2nd day.

On February 1932 and March 1932 culture and specimen of urine showed no pus or bacteria. The temperature remained normal. An intra-coccus urogram made on March 2, 1932. The outline of the left kidney pelvis much the same as before but it was well filled 25 minutes (Fig. 10, a) and completely empty 30 minutes (Fig. 10, b) whereas before the operation it had been still full outlined 1 hour and 45 minutes. Fortunately the ureter was not outlined in either film. I feel that the patient stated that she had gained 5 pounds in eight and that she felt perfectly well, as she had not for 9 or 10 years before the operation.

The fifth case was remarkable for the extreme length of the stricture. In spite of previous successes, the operative method was used with some misgivings because of the length of the stricture and especially because

the opposite kidney was severely and irreparably damaged. Nevertheless, there appeared to be no other method of dealing with the situation, which I thought then and still think provided an acid test for the procedure.

CASE 5 Mrs. A. B., aged 32 years. Severe pain in the right side began April 15, 1941. Attacks recurred about every 2 weeks, and were accompanied by chills, fever, frequency, and hematuria. Urine was cloudy at all times.

X-ray examination showed multiple large stones in the right kidney region. The urine showed many white blood cells, few red blood cells, and many bacilli.

Cystoscopy was done March 5, 1942. Urine from left kidney was clear, with no bacteria. Phenolsulfonphthalein given intravenously revealed right, 7 per cent, left 22 per cent in 10 minutes. Left pyeloureterogram showed a marked hydronephrosis, the ureteropelvic junction was funnel-shaped, but the upper ureter very small for 10 centimeters (Fig. 11). The catheter met resistance in this region.

The patient became very ill, developing severe pain in the left kidney region, accompanied by chills, sweats and high fever, indicating that infection of the left kidney had occurred. This infection persisted unabated for 8 days, in spite of large doses of sulfathiazole, and it became apparent that something radical would have to be done to save the patient's left kidney, her only good one.

Operation was performed March 13, 1942. The perineal fat was adherent and vascular. The ureter was small but thick walled with a thicker capsule than normal and numerous good sized veins coursing along it. It resembled a normal vas deferens. About 10 or 12 centimeters below the kidney it assumed a normal appearance (Fig. 12, a). The extrarenal pelvis was of moderate size and thickened (muscular hypertrophy). Ureterotomy was made in the middle of the narrowed portion. A No. 10 ureteral bulb passed upward to the kidney with great difficulty, and downward with almost equal difficulty, until it reached the normal portion of the ureter. It then went easily to the bladder. Efforts to dilate the ureter further were unsuccessful. When sufficient force was applied, the ureter split. It was felt that relief of the obstruction was absolutely necessary to the patient's welfare, as the other kidney would undoubtedly have to be removed. For this reason, the ureter was holdly incised throughout the entire length of the narrowed portion (10 to 12 cm). This converted this portion of the ureter into a narrow ribbon. The incision was extended upward a little way into the pelvis. One end of the cross piece of a No. 16 latex gall-bladder T-tube was then inserted in the pelvis. The other end barely reached the lower extremity of the ureteral incision, and was inserted into the normal part of the ureter, and held there by a suture of No. 000 plain catgut (Fig. 12, b). The ribbon of ureteral wall was then held in close

approximation to the tube by 3 sutures of No. 000 plain catgut. It did not cover more than one-third the circumference of the tube (Fig. 12, c, d). The stem of the T-tube was brought out the upper angle of the wound for urinary drainage. The wound was closed in the usual manner, with 2 or 3 rubber tissue drains.

Convalescence was afebrile and uneventful. The wound healed by first intention.

On April 14, 1942, skiodan solution was injected through the tube and the x-ray picture shown in Figure 13 was obtained. The lower limb of the T-tube was evidently occluded, but the solution flowed freely around the tube into the bladder. The tube was therefore withdrawn on April 12, 1942, 37 days after the operation. No urine drained through the incision, but the temperature rose to 100 degrees and the patient had pain in the left kidney. A No. 9 ureteral catheter was passed easily to the kidney and left in place 5 days, when it was withdrawn. There were no further symptoms, and the temperature remained normal.

On April 24, 1942, a No. 14 bulb passed to the left kidney with perfect ease, meeting no resistance at any point. The patient left the hospital April 26, 1942. Later she re-entered the hospital, and on May 19, 1942 the right kidney was removed. It was a useless, thin walled sac and contained several large stones. The convalescence was uneventful, and the patient left the hospital June 3, 1942. On July 1, 1942, the patient reported for observation. She felt perfectly well. The catheterized urine was clear, and contained no pus, blood, or bacteria. Phenolsulfonphthalein given intravenously revealed 47 per cent in 30 minutes. On August 17, 1942, a No. 14 bulb again passed to the left kidney with perfect ease. On September 9, 1942, intravenous urography was carried out. The ureter was well outlined, as shown in Figure 14, and obviously of normal diameter or greater. These findings prove beyond doubt that the new ureter is functioning in a thoroughly satisfactory way.

I was unable to find a description of any similar method for treating ureteral strictures until I found, in the 1928 edition of Keyes' *Urology*,<sup>1</sup> a recommendation for "intubation of the ureter" in such situations. Since few details were given, I consulted Dr. Edward L. Keyes personally. He gave me full particulars of a patient he had operated upon in 1915. This case is of sufficient interest to quote in full.

"An able-bodied Irish laborer, whose previous history contained nothing relating to his urinary organs, sat for 2 hours on a board covered with ice in February, 1915. Within a few hours he had a severe pain in his left loin, and the next day did not urinate. Alarmed at this, he consulted a physician,





able form. If the sutures fail to hold the tissues in their new positions until healing occurs, the operation is a failure.

In the intubated ureterotomy, no effort is made to draw the tissues into a new form, and no sutures are used. The operation depends upon the physiological repair processes of the tissues. The splint is a mold upon which the tissues, by their own proliferation, re-form the ureteral channel in normal size and shape. It must be left in place, therefore, until this proliferation is completed, and the new channel lined by epithelium. The data presented in this paper prove that this actually occurs, and that a new and normal size channel replaces the old, strictured one.

One wonders, however, whether the muscular layers of the ureteral wall also proliferate about the tube splint. If not, a considerable segment of the ureteral wall in the operative area would be devoid of muscular coats. Such a new formed ureter would be incapable of peristalsis, which might interfere with the transport of urine through the ureter. Unfortunately, it has not been possible to perform any experimental work on this problem, and no pathological material is as yet available from any of the patients who have been operated upon. One can only say that urinary drainage from the renal pelvis is free enough so that the urine has become clear and sterile in 4 of the reported cases, and possibly in the other, and that intravenous urograms give no evidence of any urinary stasis due to changes in the ureter (figs 3b, 7, 10, 14).

In the use of a ureteral or ureteropelvic splint, the size of the splint, its shape, and the length of time it is left in place are the most important points. I believe that many tubes used as splints have been too small. It seems reasonable that a tube used for this purpose should be as large as will enter the uncut, or presumably normal, part of the ureter without

fitting so tightly as to cause ischemia of its wall. It may well be that specially shaped splints, including perhaps conical ones for the ureteropelvic junction, will prove to be useful. If a splint is withdrawn too soon, it will fail of its purpose. The allowance of time for the tissues to reconstruct themselves about it should be generous, erring on the side of too long rather than on the side of too short. Three weeks may be enough, but should be regarded as a minimum. I believe it will seldom be necessary to leave a splint in place more than 4 or 5 weeks.

This method is presented in the expectation that it will prove to be a very valuable means of dealing with all kinds of ureteral and ureteropelvic stenoses, including those not amenable to any other method of treatment. Indeed, in the Jefferson Hospital urological department, operations done according to this method have entirely superseded all plastic operations on the ureter and ureteropelvic junction. We find the technique much simpler, the results much more certain. The provision of fully adequate continuous drainage for the urine during the period the splint tube remains in place is essential to success. If this is done, there are remarkably few complications and difficulties.

#### REFERENCES

1. BIDDOON, C. V. and ROBERTS, D. J. *N. England J. M.* 1935 21: 705-718.
2. CABOT, H. *Proc Mayo Clin.* 1937 1: 279-83.
3. DAVIS, D. M. *Urol Cut Rev.* 1933 37: 673-674.  
also *Tr. Western Branch Am Urol Ass.*, 1933 - 15-16.
4. GIBSON, T. I. *N. England J. M.* 1940 22: 910-917.
5. HARRIS, A. *Ann Surg.* 1935, 102: 1050-1058.
6. KEYS, EDWARD I. *Am J. M. Sc.* 1911, 161: 346-347.
7. McARTHUR, I. L. *Surg Gyn Obst.* 1925, 41: 710-711.
8. MOORE, T. D. *Am J Surg.* 1937 35: 101-117.
9. O'BRIEN, J. *Am J Surg.* 1937 35: 70-79.
10. PECK, C. H. *Ann Surg.* 1906, 53: 652-660.
11. PRITCHETT, J. T. *Surg Gyn Obst.* 1930, 65: 83-84.
12. SARGENT, J. C. *J Urol Balt.* 1937 35: 680-687.

he passed a catheter but obtained no urine. Meanwhile the pain had disappeared and the patient felt perfectly well. So for six days he did nothing, though during that time he passed not a single drop of urine. He then entered St. Vincent's Hospital.

He said he felt well but he was mentally a little troubled, his superficial capillaries a little congested, his intestines distended his blood pressure 70 his temperature normal, his left loin slightly tender but owing to distention the kidney could not be felt.

The roentgen rays showed a large left kidney but no stone. The cystoscope showed a congestion of the bladder vessels corresponding to the skin congestion. There was not a drop of urine in the bladder. The ureter catheter went 30 cm of the left ureter but drew no urine. A filiform ureteral bougie entered the right ureter for only 5 cm. and drew no urine.

I therefore immediately cut down upon the right loin but found no kidney there. I turned him over and opened the left loin and found the left kidney very large congested and tense. I incised the cortex and pushed a tube into the pelvis of the kidney liberating an ounce or more of urine.

For 10 days he was semicomatose and then recovered and made a brilliant operative recovery. For three weeks he passed large amounts of urine daily from the loin tube but none from the bladder. From the bladder shigella streptococci were obtained. A second cystoscopy revealed nothing new. Then he began to urinate as much as 700 c.c. in twelve hours. I therefore removed the tube and in a week the skin closed, whereupon the temperature went to 105, and the loin reopened, so I replaced the tube and left it in.

In July five months after the first operation, he returned to the hospital, still passing all the urine through the left loin. I reopened the loin, found the kidney very adherent and the sinus entering the center of the cortex. I mobilized the lower pole subcapsularly disclosed the adherent pelvis and the ureter moderately dilated below, narrow tight stricture at the retroperitoneal function. I opened the ureter and found that I could not pass even a probe through the stricture. I hoped to do a plastic operation but found that I could not in bilize the ureter or kidney sufficiently to do so. I therefore made another incision an inch down the ureter and introduced No. 20 F catheter through this up into the pelvis of the kidney thus splitting the stricture wide open. This tube was left in for three days. Thereafter most of the urine came from the urethra, but four days later his temperature rose to 104 and remained thereabouts for three days, when he passed a small phosphatic stone. His loin then promptly healed and his convalescence thereafter as uneventful.

Ten years later in July 1917 after a week of pain and fever in the left loin, he returned. I treated him for ten days, during which he had a regular fever each relapse of temperature being accompanied by pain in the loin and definite anuria, the longest period of anuria being twenty-four hours.

Roentgen rays showed three shadows in the pelvis of the left kidney, two of them regarded as stones. I opened the loin for the third time found the kidney so bound down that I could hardly bridge it over. I thought the old nephrotomy would and found it was one stone, stuck in the orifice of the perfect patent ureter. The confluence was entirely anastomosed except that I had to irrigate the pelvis of the kidney once through ureter catheter to reach it without drainage.

I 1919 five years after his first operation, he remained entirely well, at work and weighing 200 pounds but I have had no opportunity to make any examination except to look at his urine. It showed no pus to the eye.

Dr. Keyes again reported this case before the New York Academy of Medicine in 1922. In May 1922 the patient reported himself as still in excellent health 25 years after the operation, having had no further treatment in the meantime. Figure 15 shows an intravenous urogram taken in 1925 in which the excellent contour of the upper ureter may be noted.

I also found that McArthur in 1923 reported the repair of a completely ruptured urethra, with loss of substance. He bridged the gap with a ureteral catheter of good size. In the roentgenogram in his article it appears to be a No. 6. The kidney pelvis was drained separately by another tube. The ends of the ureter were drawn as closely together as possible but failed to meet by 3/4 inch. The splint was left in place 9 weeks. The patient became and remained well but unfortunately no postoperative urine examinations (functional tests, or roentgenograms) were reported. McArthur used this method because he had tried it successfully in reconstructing the bursae. This case is included because the operative procedure is really based on the same underlying principle as in my own operations.

Dr. Keyes assures me that he improved his operation in 1915 as I did in my first one for lack of anything better which could be done. The results, in his case and now in mine indicate clearly that it is an extremely valuable procedure that it has wide applications, and that it may be depended upon to produce good effects. The principle involved is quite different from that followed in plastic operations, in which tissues are divided and then reconstructed by sutures in a more or less



# THE INTRAPERITONEAL ADMINISTRATION OF SULFADIAZINE

With Special Reference to a Comparative Study with Sulfanilamide

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THE introduction of new sulfonamide compounds at short intervals makes it necessary not only to study their various characteristics—dosage therapeutic effect, toxicity, etc., but also to make a comparative experimental and clinical study so that we may know when each should be used and how. The synthesis and introduction of sulfadiazine by Roblin and associates, and the very favorable pharmacological and therapeutic report by Feinstein and associates led us to conduct a study of the drug. We were particularly interested in its comparative usefulness when implanted into the peritoneal cavity following operations in which contamination, such as that resulting from resection of the bowel was sustained.

The wide bacterial specificity of sulfadiazine as reported by Long, McSwain and Glenn, and others represents a distinct advantage over other sulfonamides. Wheeler and Plummer noted that the proportion of the acetlylated drug in the blood and urine was lower than with any other sulfonamide compound except one. This may explain the relatively high degree of therapeutic effectiveness with sulfadiazine. The relatively low toxicity and high blood levels per kilogram unit of dose as reported by numerous observers (3, 10, 11) is in complete agreement with the experience of the authors. Although the relative toxicity of sulfadiazine is less than that of sulfanilamide, sulfapyridine or sulfathiazole yet one of the toxic complications of sulfonamide therapy, namely renal damage (9, 13, 16, 17) occurs with a greater frequency than with sulfanilamide and at about the same frequency as with sulfathiazole. However the authors

have not observed a single instance of renal injury in the cases reported herein. In a patient not included in this report we did note oliguria which was relieved by ureteral catheterization and fluids. The patient, a young girl who previously had had one kidney removed for an actinomycotic abscess probably should have had a smaller dose or none at all. Although renal injury as manifested by one or more of such manifestations as albuminuria, blood in the urine, oliguria, anuria, etc., occurs more frequently following sulfadiazine than after sulfanilamide other toxic manifestations—e.g., headache, vertigo, fever, nausea, vomiting, mental confusion, weakness, etc.—are much less frequently encountered. Jaundice and concomitant hepatic damage which have been reported with such a high incidence with intraperitoneal sulfanilamide therapy by Jackson and Collier and others have not been encountered by us with sulfadiazine.

There are innumerable reports in the medical literature regarding the effect of the sulfonamide compounds on wound healing although some of these reports are contradictory. Most of them claim little or no detrimental effect. The recent report of Jacob and associates describing no inhibition of the growth of epithelial cells in a tissue culture media saturated with a sulfonamide compound revealed no inhibition with sulfapyridine or sulfadiazine. The greatest inhibition of cellular growth in a sulfonamide solution was in the media containing sulfathiazole. On the other hand, addition of proflavine to the media, in concentrations used clinically resulted in death of the cells. They found that the concentration of proflavine which would barely permit epithelial growth is between 1:100,000 and 1:120,000. The present 12

From the Department of Surgery, College of Medicine, University of Illinois. Aided by Grant from the Graduate School of the University of Illinois. The sulfadiazine was kindly furnished by Sharp & Doherty.

thors are inclined to attach much significance to these experiments from the standpoint of wound toxicity, interpreting them as indicating a very low degree of toxicity to tissue cells in a wound

Sulfanilamide (6, 19) is being used more frequently at the present time for intraperitoneal implantation than is any other sulfonamide, although sulfapyridine (5) and sulfathiazole (2) are also being used. If the latter drug is used, it should be implanted in the form of an emulsion (2) because of its tendency to "cake" and act as a foreign body. Regardless of which drug is used for intraperitoneal implantation it should be emphasized that the drug must be sterilized by steam pressure to prevent development of anaerobic infection. In the crystalline form, none of the sulfonamides has any deleterious effect on anaerobic organisms. The development of a fatal case of tetanus following the intraperitoneal implantation of nonsterile sulfapyridine (contaminated by the container), as reported by Atkinson, proves the necessity of sterilization.

The present authors are aware of only one report dealing with the intraperitoneal use of sulfadiazine, this is a report by Mulholland and associates (15) describing intraperitoneal use of the drug in 6 cases. They used doses ranging from 5 to 20 grams, but advised against doses as high as 20 grams. The study which we have conducted represents experimental observations which have been made on absorption time and intraperitoneal reaction in the dog, and a comparative study of 68 cases in which sulfadiazine was used intraperitoneally, and of 62 cases in which sulfanilamide was used.

#### EXPERIMENTAL METHODS AND RESULTS

In a series of 10 dogs a suspension of sulfadiazine in sterile water was introduced under aseptic technique into the peritoneal cavity by means of a trochar. The dose employed in these experiments was 0.15 gram per kilogram of body weight, which is slightly higher than the dose finally adopted for the human. This amount was suspended in 100 cubic centimeters of sterile water and introduced through the trochar. The absorption of

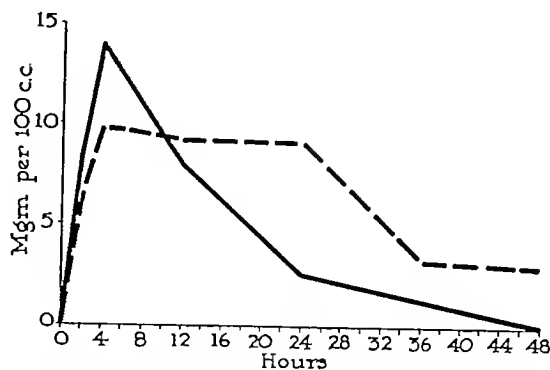


Chart 1. Note that the peak blood level of the two drugs in dogs is reached at about the same time, but is slightly higher with sulfanilamide (—). However, it falls rapidly below the sulfadiazine (—) level which is sustained longer. The dose with each drug was 0.15 gram per kilo gram, given intraperitoneally.

the drug was studied by blood level determinations at 2 to 4 hour intervals. The animals were killed at various intervals by means of intravenous nembutal, and the peritoneal cavity was inspected. Note was made of the amount of the drug which was unabsorbed. Sections for microscopic study were taken from all abdominal viscera and the peritoneum.

It will be noted in these experiments that there was prompt rise to a peak of 9.8 milligrams in 4 hours (see Chart 1), followed by a slow drop to 3.0 milligrams in 48 hours. Comparison with the curve representing the average blood levels in 5 dogs that had sulfanilamide implanted into the peritoneal cavity in the same dose, reveals that the peak is reached in the same time, but the sulfadiazine level is somewhat lower. It will be noted, however, that the blood level when sulfadiazine is used persists at a higher level, and for a longer time.

Two dogs were operated on 24 hours after injection of the sulfadiazine emulsion, and the peritoneal cavity was inspected. It was estimated that 50 per cent of the drug remained unabsorbed. The omentum was adherent to the site of the trochar puncture. Small clumps of the drug were scattered throughout the mesentery of the bowel, and in several areas they were covered by the tissue of the mesentery. Encased in the omentum were many small clumps of the drug up to 3 milli-

meters in size. These clumps were easily scraped off wherever they were attached. There was no free peritoneal fluid and there were no adhesions.

Two different dogs observed 48 hours after injection of the emulsion revealed that small masses of the drug were still encased by the omentum especially at the site of the trocar puncture. A few specks were adherent to the serosa of the bowel. No free peritoneal fluid was present. Between 30 and 40 per cent of the drug was present. In 4 days there were 6 to 10 flecks of the drug still present in 3 dogs observed. They were firmly attached in some areas, and seemed to be surrounded by the tissue of the omentum or the mesentery. A few flecks were adherent to the serosa of the small bowel. There was no gross sign of change in the serosa surrounding the site of these attachments. No free peritoneal fluid was present. The 3 remaining dogs were sacrificed in 7 days. Two small masses of the drug were encased in omentum in 1 dog and 3 similar clumps in each of the 2 others. These clumps were about a half centimeter in size. There were no adhesions except that the omentum was adherent at the site of the trocar puncture.

Microscopic sections of tissue (chiefly omentum) surrounding the sulfadiazine crystals were essentially negative in all instances except that on the 7th day a typical foreign body reaction was present with lymphocytic infiltration and foreign body giant cells.

Five dogs had sulfanilamide implanted into the peritoneal cavity by a similar technique to compare this drug with sulfadiazine. Autopsy 24 hours after implantation of the drug revealed no evidence whatsoever of the drug, all of it had been dissolved and apparently absorbed. There were no adhesions, the serosa of the bowel and all of the abdominal viscera were normal. There was no free fluid. Observations in animals 2 days, 4 days, 7 days, and 3 weeks after implantation of the drug revealed identical findings.

In addition to the experiments described, 20 dogs were operated upon and 4.5 grams of sulfadiazine placed in the peritoneal cavity directly. These experiments were done to simulate as closely as possible the method

used in the human both in the amount of the drug used and in the method of placing the drug into the peritoneal cavity. Although the actual dose adopted for use in the human was 6 grams, the animal dose per kilogram of body weight is roughly three times the human dose and the dose per square foot of peritoneal surface at least 5 times the human. All sulfadiazine used in these experiments had been sterilized by autoclaving for 15 minutes at 15 pounds pressure with a temperature of 119.6 degrees centigrade. It had previously been determined by one of us (L. W.) through animal experiments, that sulfonamides which were so heated suffered no loss of their therapeutic effectiveness.

Two dogs were sacrificed in 24 hours. It was estimated that 3 grams of the drug remained in the peritoneal cavity of each dog. The drug was again in the form of clumps adherent loosely to serosal surfaces of the bowel, liver, mesentery and peritoneum. Omentum had already surrounded the material in several areas. No free peritoneal fluid was present. Examination of 2 dogs in 48 hours revealed an estimated 2 grams of drug remaining. At the operative site of one dog there was a tangled mass of bowel adherent to the omentum and to adjacent loops. These adhesions were easily separated and there was no apparent morphological change on the serosa at the points of contact. Clumps of the drug were surrounded by the omentum in several other areas. At 72 hours examination of 2 dogs revealed about 1 gram of drug still present in each. At the point of omental attachment to the operative site in 1, there was a mass of drug measuring 2 by 3 centimeters encased in the omentum. Smaller masses up to 2 millimeters in size were adherent to the serosa of the bowel and the liver in both dogs, and the bowel in several places was loosely adherent where the drug was interposed between 2 serosal surfaces. Operation upon 2 dogs 5 days after implantation of sulfadiazine revealed omentum to be adherent to the operative site at this point the small bowel was attached to the omentum by soft adhesions. When these adhesions were separated, small masses of the drug were revealed to be interposed between the omentum and bowel and

between the loops of the bowel. On the right parietal peritoneum in 1 dog an adhesion was present between the small bowel and the parietal peritoneum. Small clumps of the drug were interposed at this adhesion also. Autopsy performed on these animals 9 weeks later revealed the omentum still attached to the operative site, but all adhesions and all of the drug clumps had completely disappeared. The adhesion to the suture line is considered incidental to the operation and not related to drug action. All viscera were normal in appearance. Autopsy on 2 dogs at 8 days revealed a loose adhesion of small bowel in each dog attached to the parietal peritoneum on the left side. Sulfadiazine clumps were present at the site of the adhesions, and several small clumps were incorporated in the omentum. In 2 dogs operated upon 10 days after implantation of sulfadiazine no crystals could be found in either case. There were no adhesions, and the loops of bowel appeared normal. Autopsy on these animals 3 months later revealed normal peritoneal cavity. Eight animals were sacrificed after 3 months. The findings in each of these animals were identical: there were no clumps of drug remaining, there were no adhesions present, and all viscera appeared to be normal.

Microscopic examinations of the tissues were negative except again a foreign body reaction was noted around the sites where the drug was surrounded by omentum or peritoneum.

Blood level determinations on 5 dogs, given 0.5 gram sulfadiazine per kilogram, are represented in Chart 2. It will be noted that with this high dose the blood level rises slowly until it reaches a peak of 40 milligrams per cent in 4 days, and then slowly falls until after a period of 8 days the blood level has reached 2 milligrams.

There were no toxic effects noted in any of the dogs following the administration of the smaller dose. With the large dose (5 times the dose adopted for clinical use) only 2 of the 20 dogs gave evidence of toxicity, this consisted of anorexia and some vomiting in the first 24 hours. All dogs made completely satisfactory recoveries from operation and reacted normally subsequently.

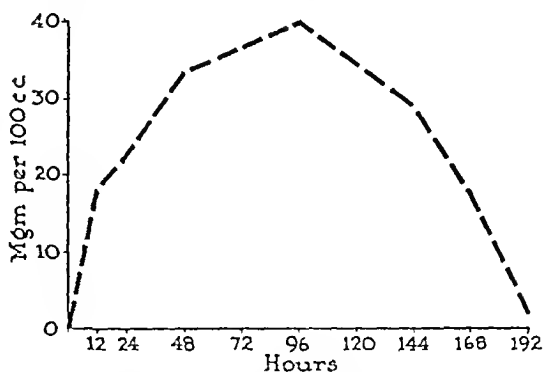


Chart 2 With such a large dose (in dogs)—0.5 gram sulfadiazine per kilogram into peritoneal cavity—the peak blood level does not occur until after 96 hours as compared to 4 hours after a dose of 0.15 gram per kilogram (see Chart 1).

#### CLINICAL METHODS AND RESULTS

Attempt was made to compare the relative efficiency of sulfadiazine with sulfanilamide when used in the peritoneal cavity of human beings following laparotomies. In general, the drugs were used only in operations in which contamination had taken place. During the period of experimentation a few clean cases were used, but the authors realize that sulfanilamide therapy in these cases as a routine is superfluous, and in routine work should not be used. Altogether sulfadiazine was used in 68 cases, and sulfanilamide in 62 (Table I). Of

TABLE I—COMPARATIVE EFFICIENCY OF INTRAPERITONEAL USE OF SULFADIAZINE AND SULFANILAMIDE

	Sulfadiazine	Sulfanilamide
Number of cases	68	62
Contaminated	52	39
Clean	16	23
Infected wounds	3*	9†
Severe	0	6
Mild	3	3
Wound disruption	1	0
Peritonitis	1	0

\*4.4 per cent. †14.5 per cent.

the 68 cases in which sulfadiazine was used 52 represented contaminated cases, and 16 clean cases. Of the 62 cases in which sulfanilamide was used 39 were contaminated, and 23 clean. In the contaminated group we included such cases as resection of the stomach, resection of the colon, gastrostomies, gastroenterostomies, resection of the ileum, etc. Cholecystectomies,



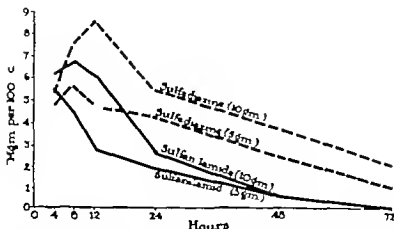


Chart 2. Note that in the drama being the peak blood level of 10th sulfadiazine is as high, in fact higher than 10th sulfanilamide; the blood level is prolonged longer 10th sulfadiazine.

herniotomies and appendectomies for non-perforated appendicitis made up most of the so called clean cases. Attempt was made to get about the same ratio of various types of operations in the 2 series. It will be noted however that there were many more contaminated cases in the sulfadiazine series indicating that the sulfanilamide series should have an obvious advantage over the sulfadiazine series.

Table I reveals that there were 3 infections in the sulfadiazine series, all of which were relatively mild. In the sulfanilamide series there were 9 infections, only 3 of which could be considered mild. In the sulfadiazine series there was an incidence of infection in 4.4 per cent of the cases, and an incidence of 14.5 per cent in the sulfanilamide series. Sulfadiazine was obviously much more effective in the prophylaxis of infection. However in the sulfadiazine series there was 1 case of wound disruption and 1 case of peritonitis which resulted fatally. The patient whose wound disrupted was an inoperable carcinoma of the stomach upon whom a gastroenterostomy had been performed. From experience we know that most instances of wound disruption occur in such patients. Since there is only 1 case of wound disruption, we doubt therefore that its incidence was anything more than a coincidental occurrence. The patient who developed a peritonitis following sulfadiazine im-

plantation in the peritoneal cavity had an operation for an intestinal fistula. A small abscess and numerous areas of acute inflammation were found in the left lower quadrant. We feel that this fatality in reality resulted from an error in the time of operation and the amount of operative work attempt was made to separate adhesions relieving a probable partial obstruction. In retrospect the process should have been allowed to resolve more before manipulation of this degree was undertaken.

There are many reports in the literature regarding the irritating effect of sulfonamide compounds on tissues, particularly regarding the drainage of serosanguinous material from wounds in which they have been implanted. We encountered one instance of excess exudation of fluid from the wound with sulfadiazine and 3 with sulfanilamide. In all instances however the drainage stopped after 3 or 4 days and the wound healed *per primam*. We consider that this drainage is usually an expression of the use of too much sulfonamide compound. In the case of the insoluble compounds such as sulfadiazine and sulfathiazole extensive drainage is probably caused by failure to distribute the drug evenly about the wound. If it is put in the wound in such large quantities in local areas that clumping can occur the residual lump will act as a foreign body or result in a dead space after the drug is

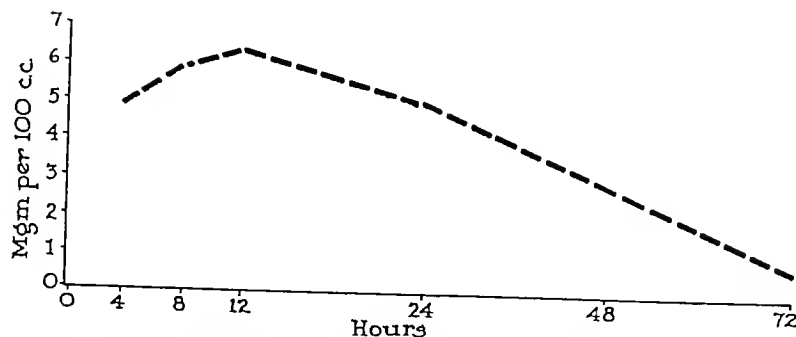


Chart 4 Average blood level (free) in the dose of sulfadiazine, 6 grams, adopted for routine use. Of the 6 grams used (in the human being) about 4 grams are placed in the peritoneal cavity and 2 in the wound

absorbed. We are firmly convinced, therefore, that the sulfonamides must be distributed very evenly over the surface of the wound or in the peritoneal cavity.

The dose used varied between 5 and 10 grams. After analyses of the results with the larger doses we could not see any evidence of a greater efficiency with such doses and, for sulfadiazine, finally decided upon a dose of 6 grams. We usually place about 4 grams inside the peritoneal cavity and utilize 2 grams for insertion in the wound. It is now fully realized that peritonitis will not develop even after a contaminating operation such as resection of the stomach, etc., unless there has been contamination of an unusual degree occurring only through carelessness. This carelessness might extend into leakage of the suture line through technical defects. On the other hand, we have seen infections of the wound develop when contamination appeared minimal. This is simply an expression of the well known fact that the peritoneal cavity tolerates contamination much better than do the tissues of the abdominal wall.

Blood level determinations were made to determine the amount of sulfonamide in the blood, and the duration of the respective levels. Chart 3 illustrates a comparison of the blood levels after the use of sulfadiazine and sulfanilamide. It will be noted that the peak level following 10 grams of sulfadiazine was 8.6 milligrams per 100 cubic centimeters, whereas the peak level following 10 grams of sulfanilamide rose only to 6.8. In the case of sulfadiazine the peak was established at 12

hours whereas with sulfanilamide the peak was established in 8 hours. This difference in the peak level is, no doubt, related to the difference in solubility. In the case of the 5 gram dose the peak level of the two drugs was practically the same but delayed slightly with sulfadiazine. In either dose it will be noted that a much higher level persisted with sulfadiazine than with sulfanilamide. As a matter of fact, after the first few hours the blood level following 5 grams of sulfadiazine was higher than following 10 grams of sulfanilamide and persisted longer. Since the effect of local implantation of sulfonamide compounds is bacteriostatic and only very slightly bactericidal (if at all), the high blood concentration for a few hours which is so characteristic of sulfanilamide *would not appear to be of any advantage*. On the contrary it would appear that a *persistent blood level* in the effective range *would be much more desirable*, since the chief effect of a sulfonamide is bacteriostatic and therefore *must extend over a long period of time to be most effective*. Under these circumstances a dose of 5 grams of sulfadiazine would appear to be fully as effective as a dose of 10 grams of sulfanilamide.

After reconsideration of the various doses we finally decided upon a dose of 6 grams of sulfadiazine for intraperitoneal use, 1 or 2 of the 6 grams being used for implantation in the wound. The peak level for this dose, as noted in Chart 4, was 6.2 milligrams per 100 cubic centimeters, and occurred at 12 hours. The amount gradually diminished to 3.2 at 48 hours and dropped to slightly more than 1

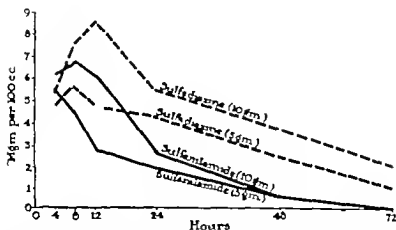


Chart 1. Note that in the human being the peak blood level 1 lb sulfadiazine is as high, in fact higher than 1 lb sulfanilamide; the blood level is prolonged longer with sulfadiazine.

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Sulfadiazine has another advantage over sulfanilamide in so far as a given blood level is reached and maintained with a smaller dose than with sulfanilamide. Toxic symptoms such as headache, nausea, vomiting, fever, cyanosis, etc., are more common with sulfanilamide but renal complications are more common following sulfadiazine therapy. However, in the series herein reported we did not observe a single instance of renal complication. We are convinced that *if high doses of sulfadiazine are to be given, a fully adequate fluid intake (3000 cc per day for an adult) must be maintained*

Sulfadiazine has a much wider range of specificity than sulfanilamide, being effective against the hemolytic streptococcus (3, 10, 11) as well as many other bacteria. Although the peak level may be reached a few hours earlier with sulfanilamide than with sulfadiazine, this would not appear to be an advantage from a prophylactic standpoint, although it would, no doubt, be of advantage if an infection were already present.

About the only disadvantage possessed by sulfadiazine would appear to be its persistence in the wound for several days—a feature caused by its relative insolubility. However, we are by no means convinced that this feature is a disadvantage, as long as the drug is distributed evenly throughout the peritoneal cavity and wound, and not dumped in one place, thus creating a foreign body effect. It appears likely that “lumping” of the drug would likewise be disadvantageous in the case of sulfanilamide, but through another mechanism, namely, exposure of tissue to a concentrated solution of the drug, resulting from its greater solubility.

#### SUMMARY

Sulfadiazine crystals were implanted in the peritoneal cavity and wounds of 68 patients operated on for various lesions, most of which resulted in peritoneal contamination. A similar study in which 62 patients were used was conducted with sulfanilamide. In the series

studied we obtained an incidence of wound infection of 4.04 per cent with sulfadiazine and 14.05 per cent with sulfanilamide. Since there were more contaminated cases in the sulfadiazine series it appears definite that at least in our experience, sulfadiazine was superior to sulfanilamide in the prevention of wound infection. However, in the sulfadiazine series there was 1 wound disruption, and 1 case of fatal peritonitis. We believe, however, that these 2 cases are coincidental, and doubt that they are related to the use of sulfadiazine. No toxicity of any kind was noted with the sulfadiazine, neither was there any evidence of delay in wound healing. After study of blood levels, etc., we finally adopted 6 grams as the routine dose, we implanted 4 grams in the peritoneal cavity, and 2 grams in the wound at the end of the operation. It should be emphasized that all sulfonamides should be sprinkled evenly over the surface of wounds. Particularly is this true of the less soluble compounds such as sulfadiazine.

Our studies on animals, as well as on human beings, revealed a much more persistent blood level with sulfadiazine than with sulfanilamide. In our observations on the human, we noted that the blood level following 5 grams of sulfadiazine intraperitoneally was higher than the blood level following sulfanilamide.

In our experience, sulfadiazine is less toxic than sulfanilamide. We believe that the greater persistence of the blood level of sulfadiazine over sulfanilamide makes the former drug superior to the latter for implantation in the peritoneal cavity and wound following laparotomy, particularly when we consider that the beneficial effect of the sulfonamide compounds is primarily bacteriostatic and only slightly bactericidal.

In our experience the use of sulfonamides in wounds contaminated by resection of bowel has resulted in a much lower incidence of infection, sulfadiazine being superior to sulfanilamide.

If sulfonamide action is desired for a few days following operation and intraperitoneal use of the drug therapy must be resumed more rapidly with sulfanilamide (usually subcutaneously or intravenously in 0.5 to 0.9 per cent solution in physiologic saline solution).

milligram per 100 cubic centimeters at 72 hours.

#### ANALYSIS OF RESULTS

As noted in Charts 1 and 2 the type of curve following local implantation of a sulfonamide compound varies markedly with the dose. As the dose is increased the peak level is delayed. There are likewise additional factors controlling the type of curve. The amount of surface area over which the drug is implanted is probably one of the most important of these remaining factors. However even though these factors be controlled there is still a wide variation in the peak level and persistence of blood levels with all sulfonamide compounds; this fact has been observed by numerous investigators. In Chart 1 it will be noted that following the implantation of 0.15 gram of sulfadiazine per kilogram of body weight in a dog the blood level rose to 9.8 milligrams per 100 cubic centimeters and persisted for 48 hours, at which time it had dropped to 3.8. This level is not significantly different from the level in a human being with an equivalent dose. There is one difference however in so far as the peak level in the dog is reached in 4 hours instead of 12 hours in the human being. This increase in the absorption is related to animal species.

Sulfadiazine persists in the peritoneal cavity of the dog for several days. At points where the drug has collected or was not spread out evenly over the peritoneal surface the omentum becomes adherent as it would around any foreign body. However observation of these animals after absorption of the drug always revealed complete obliteration of these adhesions. They were never dense in the first place and in the authors' opinion would not result in intestinal obstruction. No free fluid beyond normal quantities was ever noted in the abdominal cavity of the animals. At no time did we find evidence of lack of healing either in animals or in human beings.

As stated previously the incidence of infection in our clinical experience was greater following the use of sulfanilamide than following

sulfadiazine. We believe the difference in incidence is sufficiently great to be more than coincidental and are convinced that, at least in our experience, sulfadiazine was superior to sulfanilamide. When sulfadiazine is used it should be spread evenly over the surface so that it will not accumulate in large clumps. A foreign body reaction in the omentum surrounding clumps of sulfadiazine was noted in our experiments. Sulfonamides including sulfadiazine have been used experimentally on brain tissue by Russell and Falconer, Tadd and German and others, and the same foreign body reaction observed, but without any significant inflammatory reaction.

A recent preliminary report by Fox suggests that sodium sulfadiazine might be used in place of sulfadiazine for implantation in wounds. The authors realize that faster absorption would be obtained but doubt whether the difference in a few hours would be significant since the drug is primarily bacteriostatic and not bactericidal. It appears obvious that if the drug used for implantation in tissues is extremely soluble, the tissues will be exposed to a very hypertonic solution and thereby might be damaged.

Opinions would no doubt differ as to the optimum characteristics desired in a drug for intraperitoneal use. However all would agree that such a drug must be relatively free from toxicity in effective doses. Sulfanilamide and sulfadiazine each would qualify in this respect. We are of the opinion that a drug which has a blood level of prolonged duration is superior to one with a shorter one. Since the primary mode of action of the sulfonamides is because of their bacteriostatic action and not bactericidal effect we can see no advantage in a relatively high blood level (perhaps above the effective therapeutic range) if it recedes rapidly (in a few hours) to a level below the effective range. If this reasoning is sound, sulfadiazine has an advantage over sulfanilamide since the blood level following the latter is much less persistent. Naturally the dose of sulfanilamide might be repeated, but it cannot be implanted into the peritoneal cavity or wound except at the time of operation. Any of the drugs may be given parenterally (sulfanilamide by vein and subcutaneously) and

\*Since analyzing the data herein given, about 30 additional cases of subperitoneal implantations of sulfadiazine have been observed. There has not been a single instance of post-operative intestinal obstruction in either series.

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than with sulfadiazine. The common method of administering sulfadiazine under such circumstances is to give sodium sulfadiazine intravenously (e.g. 3 grams twice daily)

## REFERENCES

1. ATKINSON E. C. Brit. M. J. 942, July 4, 1944.
2. CRAMER, S. A., HARRIS, T. N., SCHUM, W. F. and THOMPSON, L. E. J. Am. M. Ass. 942, 9, 34.
3. FERGUSON, W. H., WILLIAMS, R. D., WOLFE, R. T., HENNINGSON, L., and CROWLEY, A. L. Ball. Johns Hopkins Hosp. 940, 67, 427.
4. FOX, C. L. Arch. Surg. 942, 45, 754.
5. GARDNER, R. H. Lancet, Lond., 942, 95.
6. METCALF, R. S. J. Am. M. Ass. 94, 6, 330.
7. JACKSON, H. C., and COLLIER, F. A. J. Am. M. Ass. 942, 8, 95.
8. JACOBY, F. M. P. B. and WILKINSON, E. A. Brit. M. J. 94, 49.
9. KRITZER, W. A. and CAMPBELL, J. A. J. Am. M. Ass. 942, 9, 704.
10. LOVELL, P. H. J. Am. M. Ass. 94, 6, 375.
11. NIQUART, 94, 20, 49.
12. MCDONALD, R. and GLENN, I. Arch. Surg. 94, 44, 33.
13. ROWLEY, R. D., WILLIAMS, R. D., WILSON, P. S., and ENGLISH, J. P. J. Am. Chem. Soc. 64, 6, 2007.
14. RAYNER, S. L. J. Am. M. Ass. 1942, 9, 426.
15. RUSSELL, D. S. and FALCOW, M. A. Lancet, Lond. 940, 2, 100.
16. RYAN, J. D., BAUM, E. and METCALF, J. H. J. Am. M. Ass. 942, 9, 494.
17. SCHULTZ, J. W., KENDLER, F. P. and VITTORE, J. J. J. Am. M. Ass. 942, 9, 4.
18. SETTON, H. B. J. Am. M. Ass. 942, 19, 19.
19. TAYLOR, M. and GLENN, W. J. Ark. J. Med. 4, 30.
20. THOMPSON, J. M., BRADY, J. A. and WALKER, J. M. Surg. Gyn. Obst. 94, 7, 7.
21. WHARTON, C., and FLETCHER, V. Ann. Int. M. 94, 6, 269.

# A STATISTICAL METHOD FOR EVALUATING THE RESULTS OF TREATMENT FOR PEPTIC ULCER

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**D**URING the past two decades the various methods of treating peptic ulcer, both medical and surgical, have been marked by persistent and widespread disagreement regarding their merits. As yet a certain cure for this disease remains unknown, for none of these therapeutic measures can assure the patient against a recurrence of his disorder. It happens not infrequently that a patient remains free of symptoms for 20 or 30 years, only to experience a recurrence of ulceration after such a long interval. Hence, the effect of such therapeutic procedures cannot be evaluated on the basis of definite and permanent cures but only on the chances of the patient's remaining free from recurrence for a limited time interval. Furthermore, the measure of therapeutic efficacy is influenced by a multiplicity of causes, and for this reason any attempt to evaluate it quantitatively resolves itself of necessity into a statistical (i.e., biometrical) problem.

Now, statistics in a technical sense is not merely the compilation of data from hospital records and the computation of "percentages"—by some haphazard procedure. Rather, it implies the utilization of a logical, well conceived technique for the numerical representation and evaluation of such case records, according to certain well established mathematical principles known as *statistical methods*.

The essence of this technique is very well expressed by the following quotation from A. Bradford Hill's *Principles of Medical Statistics*: "Whereas the laboratory worker can frequently exclude variables in which he is not interested and confine his attention to one or more controlled factors at a time, the clinician and social worker have to use records which they know may be influenced by factors which they cannot control but have essentially to be taken into

account. The essence of the statistical method lies in the elucidation of the effects of these multiple causes."

The statistical method is required in the interpretation of figures which are at the mercy of numerous influences, and its object is to determine whether individual influences can be isolated and their effects measured. The essence of the method lies in the determination that we are really comparing like with like, and that we have not overlooked a relevant factor which is present in Group A and absent from Group B."

In short, statistics are "quantitative data affected to a marked extent by a multiplicity of causes" and statistical methods are "methods especially adapted to the elucidation of such data" (Yule and Kendall).

Failure to recognize this fact is in no way restricted to the ulcer problem, but it exists in virtually every similar field of clinical investigation. We feel that the present confusion in evaluating different therapeutic procedures for peptic ulcer must be ascribed in a great measure to the disregard of this basic idea regarding methodology. Hence, any further efforts in this direction must be approached in the light of a statistical technique which fulfills the requirements of accepted "statistical theory." Unless this premise be generally accepted, there is no reason to expect that future efforts will be any more productive of conclusive results than those of the past have been.

In order to grasp the implications of this point of view more fully, let us review the procedures which have hitherto been employed for evaluating surgical methods for ulcer therapy. It is only by trial and error that clinicians have come to recognize the manifold, and sometimes intangible, nature of the factors which influence the quantitative appraisal of the results of treatment. As fallacies in the methods for evaluating results have come to light, efforts have been made to correct them, but the evolutionary nature of this process has not been generally recognized because each investigator focused attention

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This investigation was supported in part by a grant from the Friedsam Foundation

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only on a particular weakness which he perceived in the methods of his predecessors. Thus it was early recognized that, in the case of a disease like peptic ulcer in which there is no certainty of cure the post-therapeutic time exercises a most important influence on the numerical evaluation of success or failure. Likewise the need for careful personal and continuous follow-up observation for the detection and reliable interpretation of recurrent complaints was not appreciated until experience had revealed that peptic ulcer is a disease of remissions and recrudescences, and that its manifestations may be simulated by other disorders. In the course of time it became apparent that the character of the clinical material selected for treatment and for study exerts most important influence on the measures of the risk and of the end results of treatment. Throughout the years, various observers have employed different criteria for evaluating the effectiveness of peptic ulcer therapy. As a consequence there has been no standardization of criteria so as to permit of valid comparison of results reported by different clinics. And finally little consideration has been given to the element of chance or probability which enters into the results obtained with any single group of patients considered as a sample of the universal population of all such patients. I.e. the concept of random sampling has been generally neglected.

Specifically the following are the more striking weaknesses in the methods which have been employed in studying the end-results of treatment.

Many of the earlier reports disregarded the ever present possibility of a recurrence and the importance of postoperative time in following cases. This is well illustrated by the frequent report of results in such terms as cases followed for one to ten years—80 per cent cured.

2. When the importance of the time factor first came to be recognized, therapeutic success was sometimes evaluated on the basis of the results after a poorly defined time interval. Thus, one writer claimed his follow-up data on the basis of early and late results—less than or more than one year postoperative—another employed 'no less than a 5 year fol-

low-up, and a third group of investigators used the time interval of their own actual experience as a basis for measuring their surgical results. In all these reports, however the time was represented by an average or a limiting value for the entire group and not by a time interval which held for all the patients individually. e.g. cases for an average of 7.1 years—none less than 2 years and some for as long as 15 years. In other words the sample population of the entire study was made up of individuals who had survived the operation for different lengths of time and therefore were not truly comparable in this respect. Is another instance, in one of the best studies of the results of surgery for peptic ulcer that we know of average follow-up periods of 5.4, 6.3, 3.3 etc. years are given, whereas the observations on which these averages were based varied from 1 to 15 years.

3. In an effort to circumvent the fallacy of conclusions based upon a follow-up of inadequate duration some writers adopted an arbitrary period of observation for every case in the group as the necessary *lower limit* for establishing the permanence of a therapeutic result. e.g. cases followed for a minimum of five years. The validity of such a limited interval as an overall measure of success has always been assumed without any formal justification.

4. The latest and most constructive improvement in statistical technique for evaluating ulcer therapy is contained in the principle termed "follow-up in continuity" by St. John and his associates (3, 4). According to this principle every patient must be seen at repeated and fairly regular intervals, so that the course of his postoperative history can be followed with the progress of time. One very important consequence of this procedure might be the charting of a trend curve which shows the rate of development of failures at various times after operation. The authors failed to utilize this possibility, however, and merely calculated their results in terms of an average follow-up time.

The foregoing review of the various ways in which observers have estimated the results of therapy for peptic ulcer indicates clearly the weaknesses and fallacies of such statistical data. In view of this situation we set ourselves

the problem of devising a statistical procedure which will avoid most of the weaknesses in the methods previously employed for this purpose. The result of our labors has been a method for measuring the success of any therapeutic procedure for a nonmalignant disease which may recur at any time during the life of the patient. In the course of this work we formulated a series of fundamental conditions which must be adhered to in order to insure statistical validity, and we shall discuss these requirements before presenting the method in detail.

#### FUNDAMENTAL PRINCIPLES UNDERLYING THE METHOD

1 Every patient should be seen at follow-up personally and periodically (3 to 6 months), and his condition should be appraised at least once a year. In this way we obtain the number of *new failures* which have developed in the course of each year, and the corresponding total number of patients observed. From these data it is possible to construct a cumulative curve which reflects the timetrend of the recurrences, i.e., a curve for the total number (or %) of recurrences for 1, 2, 3, etc. years after operation.

2 All patients operated upon during any one calendar year (e.g., January through December, 1924) are said to fall within the same "surgical year." All observations made during the same postoperative year, *irrespective of the surgical year*, are said to fall within the same "postoperative" or "follow-up year." For example, the result in patients operated upon in 1924 and in 1930, and appraised in 1926 and in 1932 respectively, are all classified as falling in the second follow-up year. Thus, we may combine data for different surgical years provided only that the groupings are made according to follow-up rather than chronological year. Furthermore, suppose it is desired to study the therapeutic effects of an operation over a period of 15 years (or 10 years, or 5, as the case may be)—that is, the entire duration of the trend curve is set at 15 years. Then every case included in the sample population for this study must have been followed for at least this length of time. Thus, if results are available on operations performed

from 1923 through 1941, and it is desired to study the postoperative course of the disease for 15 years, then the population sample chosen for this study must exclude cases of all patients operated upon after 1926—for these latter cases obviously would not yet have reached a 15 year follow-up by 1941. All patients operated upon in 1927 or thereafter afford the possibility of an independent study of shorter duration. Thus, the patients operated from 1927 through 1931 constitute a sample population which is valid for a 10 year study (but no longer). Such a 10 year trend curve may be compared with the corresponding portion of the 15 year curve in order to obtain some notion of the variation from sample to sample (i.e., the sampling error). Of course, if only a 10 year curve were desired in the first place, it might have been obtained from the combined data for 1923–1931, by discarding all data beyond the tenth follow-up year. In a similar manner the data for patients operated upon in 1932–1936 afford an opportunity for a 5 year study, which may be compared with the two previous samples, but only for this duration. By this method we have eliminated the fallacy of the "average period of follow-up." At the same time, the entire mass of data from 1923 to date has been broken down into 3 independent sample populations which, by their comparison, afford an excellent opportunity for a study of the internal consistency of the statistical procedure.

3 In actuality, such a year-by-year follow-up is impossible for every patient included in a group of surgical survivors, because a considerable proportion of them become lost to observation at varying times after the operation. The reasons for this failure to return for examination are manifold: (1) the patient may migrate to another community, (2) being free of symptoms, he may become indifferent to the requests for a follow-up, (3) sometimes, if his condition remains unimproved after a few visits to the follow-up clinic, he will seek relief elsewhere, (4) the patient may die without our knowledge. Concerning the therapeutic fate of patients in these four categories, we can make no certain statement. *We believe that the incidence of failure among this group of patients*

is no greater than among those who return to follow-up year after year (the observed group) and it may be even less. Substantiation of this premise is impossible nevertheless we believe that it is valid with a high degree of probability. Our reason for this belief is as follows. Patients sometimes return with recurrent symptoms after many years of absence from follow-up. When asked the reason for their failure to return during the interim, they have consistently stated that, being well, they saw no point in coming back. It is sometimes contended by other writers that patients are lost to follow-up chiefly because they seek treatment elsewhere for the relief of recurrent symptoms. In our experience however such a patient will return at least once to report his recurrent symptoms to us before going to another institution and therefore this contention is not a valid criticism of our premise.

This problem of the 'unfollowed case' is as difficult in medicostatistical studies as it is universal. It is impossible to determine the true percentage incidence for the entire sample when the history of a large proportion of that sample is unknown. It is possible however to determine the upper and lower limits of a range within which this 'true' percentage must fall. Thus if the number of failures observed in any one postoperative year be divided by the total number of patients who survived the operation initially, the ratio is the minimum possible percentage incidence of failure in this sample. It is evident that the true percentage cannot be less than this and is almost certainly greater by reason of the unrecorded failures. On the other hand, if we divide the number of failures observed in this postoperative year by the number of patients who actually returned to follow up, we obtain a maximum estimate of the true incidence. This percentage incidence is precise for the observed group alone and therefore—by the premise formulated in the previous paragraph—the true incidence for the entire group of cases is no greater than this value and it may even be less than it. These maximum and minimum measures of percentage incidence afford a pair of trend curves between which the 'true' trend curve must in all proba-

bility fall. For practical purposes we calculate the median average for each such pair of values, and we regard the resulting median trend curve as a better estimate of the true one than either of the others.

4 Any study concerned with 'failure' of a therapeutic procedure for peptic ulcer necessitates a careful definition of the criteria of failure employed. What may be considered as adequate criteria, however is a moot question which will be discussed in detail in another publication, since its solution does not materially influence the principles underlying our present statistical procedure. Suffice it to state that for the present purpose—which is merely to illustrate a statistical technique—we have defined a failure as the case of any patient who reveals *any* evidence of recurrent ulceration, or who manifests symptoms which may reasonably be ascribed to such.

It frequently happens that a patient with a recorded recurrence fails after a time to return for further follow-up observation. Such patients are treated as though they had returned each year on the principle that once a failure, always a failure. As such, they are included in the number of patients who in every postoperative year for the entire duration of the study.

#### STATISTICAL PROCEDURE

In order to describe and illustrate our method for analyzing the results of therapy for peptic ulcer we have employed the data from the Mount Sinai Hospital for patients with duodenal ulcer who were subjected to subtotal gastrectomy during the years 1921-1934. This material covers an interval of 12 surgical years and affords a maximum follow-up time of 17 years. Since this report is concerned only with statistical methodology, a detailed description of the factors characterizing the clinical material is not requisite. Such a description will be presented later in a clinical report dealing specifically with the factors influencing the results of the operation at this hospital.

Our first concern was the determination of the recurrence-trend curve for at least 15 years after operation. For this purpose we take

TABLE I—ANNUAL INCIDENCE OF RECURRENCE OF ULCERATION FOLLOWING SUBTOTAL GASTRECTOMY FOR PRIMARY AND SECONDARY DUODENAL ULCER, SAMPLE A, SURGICAL YEARS 1923-1925

Year of operation	1923	1924	1925	Totals
No of survivors	18	41	38	97
Postoperative year	Summary of annual follow-up by postoperative years No recurrences—No cases followed			
1	0-10	0-36	0-32	0-78
2	0-10	1-34	0-25	1-69
3	2-10	1-32	0-22	3-64
4	0-10	0-27	0-21	0-58
5	1-10	0-25	0-21	1-56
6	0-9	1-23	0-21	1-53
7	0-8	0-22	0-19	0-49
8	0-8	0-20	0-19	0-47
9	0-8	0-19	0-18	0-45
10	0-8	0-19	1-17	1-44
11	0-8	0-19	0-17	0-44
12	0-8	0-19	0-16	0-43
13	0-8	0-17	0-16	0-41
14	0-8	0-17	0-14	0-39
15	0-8	0-17	0-11	0-36
16	0-8	0-15	0-11	0-34

lated the results for the surgical years 1923-1925 inclusive (sample A), disregarding all observations made after the 16th follow-up year (Table I)

The first line of the chart contains the surgical year—when the operation was performed. The second line contains the number of patients who survived operation in each surgical year, the sum of these represents the total number of survivors included in the entire sample population. The third line contains the number of new recurrences detected during the first follow-up year for each of the 3 surgical year groups, irrespective of the calendar year of observation. The corresponding number of patients who actually returned to follow-up is likewise presented in this line, after the dash. The totals for each of these two items respectively (in the last column) gives the total number of failures (o) and the total number of cases observed (78) in the first follow up year for the entire sample A. The

TABLE II—ANNUAL AND CUMULATIVE PERCENTAGE INCIDENCE OF RECURRENCE AFTER SUBTOTAL GASTRECTOMY FOR PRIMARY AND SECONDARY DUODENAL ULCER, SAMPLE A, SURGICAL YEARS 1923-1925

Follow up year	No survivors	Cases followed		Annual incidence of new recurrences			Cumulative incidence of recurrences		
		No	%	No	Min %	Max %	Min %	Max %	Med %
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
1	97	78	80.4	0	0	0	0	0	0
2	97	69	71.1	1	1.0	1.4	1.0	1.4	1.2
3	97	64	66.0	3	3.1	4.7	4.1	6.1	5.1
4	97	58	59.8	0	0	0	4.1	6.1	5.1
5	97	56	57.7	1	1.0	1.8	5.1	7.9	6.5
6	97	53	54.6	1	1.0	1.9	6.1	9.8	8.0
7	97	49	50.5	0	0	0	6.1	9.8	8.0
8	97	47	48.5	0	0	0	6.1	9.8	8.0
9	97	45	46.4	0	0	0	6.1	9.8	8.0
10	97	44	45.4	1	1.0	2.3	7.1	12.1	9.6
11	97	44	45.4	0	0	0	7.1	12.1	9.6
12	97	43	44.3	0	0	0	7.1	12.1	9.6
13	97	41	42.3	0	0	0	7.1	12.1	9.6
14	97	39	40.2	0	0	0	7.1	12.1	9.6
15	97	36	37.1	0	0	0	7.1	12.1	9.6
16	97	34	35.1	0	0	0	7.1	12.1	9.6

Column (6)=column (5) divided by column (2), column (7)=column (5) divided by column (3) column (10)=one-half the sum of columns (8) and (9)

fourth and subsequent lines contain the same arrangement of data for each of the remaining follow-up years

The totals from Table I were next transferred to Table II, for the calculation of the various percentage values. Column 2 contains the total number of survivors of the operation included in this sample. The number of patients observed each postoperative year<sup>1</sup> is given in column 3, and the corresponding percentage, relative to the total number of survivors (i.e., the follow-up percentage), in column 4. The next column contains the actual number of recurrences detected in each follow-up year. When this number is divided by the number of survivors (from column 2) it gives the *minimum percentage recurrence* (column 6),

<sup>1</sup>As already stated this number includes all previous recurrences regardless of whether they actually returned to the follow up clinic after recurrence had been detected.

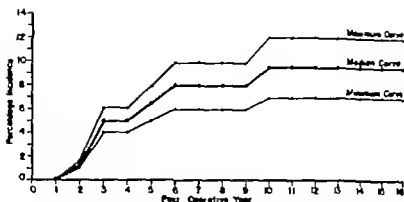


Fig. 2. Trend curves for the cumulative incidence of recurrence of ulceration following subtotal gastrectomy for duodenal ulcer. Sample A covering surgical years 1926-1935. Number of operative survivors 97.

and when it is divided by the number of patients actually seen (from column 3) we obtain the *maximum percentage recurrence* (column 7).

The next step is to accumulate the data so that they reflect the total extent of recurrence from the first through each indicated follow up year in turn. This must be done in terms of the percentage values and

TABLE III.—ANNUAL INCIDENCE OF RECURRENCE OF ULCERATION FOLLOWING SUBTOTAL GASTRECTOMY FOR PRIMARY AND SECONDARY DUODENAL ULCER. SAMPLE B, SURGICAL YEARS 1926-1930

Year of operation	1926	1927	1928	1929	1930	Total
No. of survivors	37	37	36	39	37	186
Post-operative year	Summary of annual follow up by postoperative years No. recurrence—No. cases followed					
1-1	0-34	0-43	0-28	0-36	0-27	
1-24	0-27	0-30	0-26	0-24	0-22	
0-20	0-13	0-30	0-26	0-8	0-13	
0-25	0-11	0-20	0-23	0-23	0-	
0-23	0-	0-00	0-0	0-22	0-12	
0-11	0-	0-1	0-	0-17	0-00	
1-14	—	0-23	0-00	0-1	0-20	
0-	0-10	0-20	0-13	0-27	0-07	
0-	0-	0-1	0-1	0-27	0-20	
10	0-20	0-1	0-1	0-1	0-0	
0-10	0-10	0-	0-1	0-	0-20	

not the frequencies (the actual numbers of cases) themselves, because the former constitute an adjusted value of the latter—adjusted for the variation in number of cases followed each year. Thus, for example the minimum percentage of recurrence (column 8) for the 7th follow-up year is obtained by adding together the percentage values from column 6 for each of the first 7 such years. The

TABLE IV.—ANNUAL AND CUMULATIVE PERCENTAGE INCIDENCE OF RECURRENCE AFTER SUBTOTAL GASTRECTOMY FOR PRIMARY AND SECONDARY DUODENAL ULCER, SAMPLE B, SURGICAL YEARS 1926-1930

Follow-up year	Cases followed		Annual incidence of new recurrences		Cumulative incidence of recurrence			
	No.	%	No.	%	Max.	%	Min.	%
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
186	173	93						
86	64	74					6.4	
186	22	12			8			
186	69							
186	118	63				8		
170	106	62						6.2
86	103	12				16.4		
86	97	11						
186	90	48						
10	86	81					8	
186	76	41						

Column (5) recurrence (divided by column (2) annual incidence)  
(1) divided by column (2) column (6) would be the sum of column (5) and (9)

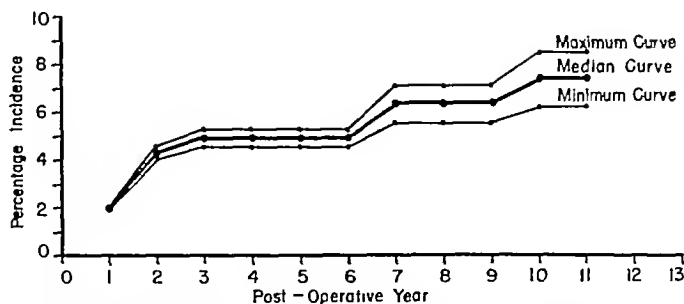


Fig 2 Same as Figure 1 Sample B covering surgical years 1926-1930  
Number of operative survivors 180

maximum percentage of recurrence (column 9) is calculated similarly from the data of column 7. And finally, the median average of these upper and lower limits is recorded in the last column.

The significance of the foregoing data is best appreciated from their graphic representation. Such plots for the cumulative incidence of recurrence are shown in Figure 1. A similar study on a second sample population (sample B, 1926-1930), which permits of an analysis of results over an 11 year period, is presented in Tables III, IV and Figure 2. A third sample covering the years 1931-1934 (sample C) was available for a 7 year period of study.

Although this postoperative period is of relatively short duration, the data afford opportunity for comparison with other material of like duration, taken from samples A and B, and so this third sample has also been included in the present study (Tables V and VI, Figure 3).

#### ANALYSIS OF THE TREND CURVES

In order to comprehend the characteristics of the cumulative trend curves, let us analyze that for sample A in detail (Fig 1). The maximum and minimum incidence curves both rise with moderate abruptness and then flatten out to form typical plateaux. The two curves have essentially the same shape, the divergence be-

TABLE V—ANNUAL INCIDENCE OF RECURRENCE OF ULCERATION FOLLOWING SUBTOTAL GASTRECTOMY FOR PRIMARY AND SECONDARY DUODENAL ULCER, SAMPLE C, SURGICAL YEARS 1931-1934

Year of operation	1931	1932	1933	1934	Totals
No of survivors	30	24	7	10	100
Post operative year	Summary of annual follow-up by postoperative years No recurrences—No cases followed				
1	2-16	0-23	0-27	0-0	2-95
2	0-31	1-22	1-16	0-0	1-59
3	0-26	1-22	1-4	1-0	3-51
4	0-6	0-0	0-24	0-0	0-70
5	0-23	0-16	0-4	0-0	0-72
6	0-10	1-15	0-22	0-7	1-61
7	0-10	0-15	0-10	0-7	0-60

TABLE VI—ANNUAL AND CUMULATIVE PERCENTAGE INCIDENCE OF RECURRENCE AFTER SUBTOTAL GASTRECTOMY FOR PRIMARY AND SECONDARY DUODENAL ULCER, SAMPLE C, SURGICAL YEARS 1931-1934

Follow up year	No of survivors	Cases followed		Annual incidence of new recurrences			Cumulative incidence of recurrences		
		No	%	No	Min %	Max %	Min %	Max %	Med %
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
1	100	95	95.0	2	2.0	2.1	2.0	1	1
	100	83	83.0	2	2.0	3	4.0	4.4	4
3	100	81	81.0	3	3.0	3	7.0	5.1	7.6
4	100	79	79.0	0	0	0	7.0	8.1	7.6
5	100	72	72.0	0	0	0	7.0	8.1	7.6
6	100	63	63.0	1	1.0	1.6	8.0	9.7	8.9
7	100	60	60.0	0	0	0	8.0	9.7	8.9

Column (6) = column (5) divided by column (2). Column (7) = column (5) divided by column (3). Column (10) = one half the sum of columns (8) and (9).

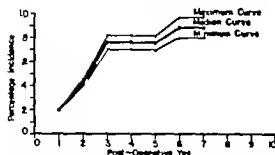


Fig. 3. Same as Figure 2, Sample C covering surgical years 93-934. Number of operative survivors 60.

tween them being a reflection of the loss of follow up patients. Hence the median curve also possesses the same general form: its plateau starts at the 10th year which means that all of the recurrences became manifest up to that time and that none were observed during the last 6 years of follow up. This total median incidence of recurrence is 9.6 per cent and of this total about two-thirds (6.5%) occurred during the first 5 years after operation and one-third (3.1%) during the second 5 year postoperative period. Similar characterizations might be made for any other grouping of years (e.g., 4, 8, 12 and 16) but the 5 year intervals are those in common use.

The curves of sample B (Fig. 2) possess essentially the same characteristics although a continuation of only 1 year beyond the 10th is insufficient to establish the existence of a plateau. The total median incidence of recurrence through the 10th year is 7.3 per cent; the proportion of these recurrences in the first 5 year period is again about two-thirds (4.9 per cent) and for the second such period it is one-third (2.4%). It will be noted that the divergence between the maximum and minimum curves at the 10th year is appreciably less for sample B than for sample A (2.1% as compared with 4.0%) thus making the estimate of 'true incidence in the former more reliable than in the latter. Obviously this difference in spread for the two samples is a reflection only of the difference in their relative completeness of follow up. As for sample C (Fig. 3) analysis of these characteristics is as yet impossible because of the limited duration of the experience.

In order to compare the results from these 3 samples more effectively, their median curves are presented together in Figure 4. The general similarity in shape is apparent, although certainty on this score must await the passage of sufficient time (at least 13 or 14 years of study in each instance) to insure the existence of the plateau. The question naturally arises: is the difference in height of these curves indicative of a significant difference in their respective incidences of recurrence, or is it merely a reflection of random sampling? (For an application of this concept see the Evaluation of Study.) For instance, the 10 year incidence of recurrence for samples A and B is 9.6 and 7.3 per cent respectively, with a difference of 2.3 per cent between them. To determine whether this difference is statistically significant we may apply the statistical test generally used in such circumstances (see the Appendix). The result indicates that this difference is not significant and arises only by reason of the variation which may be expected from sample to sample of the same population. A similar test applied to the cumulative 5 year incidence from these two samples yields a difference of 1.6 per cent (6.5-4.9) which is likewise not significant by this statistical criterion. The third sample, which has been under observation for only 7 years, yields a 5 year incidence of recurrence of 7.6 per cent, but the difference between this and 4.9 per cent for sample B is also not significant. In this way we have established partially the consistency of these 3 sets of data, or their statistical homogeneity.

#### EVALUATION OF STUDY

Our procedure for evaluating the therapeutic end results of surgery for peptic ulcer involves certain definite departures from previous methods. The principles upon which our procedure has been based are as follows: (1) Rigorous adherence to a study of each case at regular time intervals (i.e., a record of the year-by-year destiny of each patient) is essential. This must be based on a carefully defined criterion of failure. (2) Such periodic follow up must be continued as long as the patient lives. (3) In grouping cases for statistical analysis, a limiting minimum duration of 14

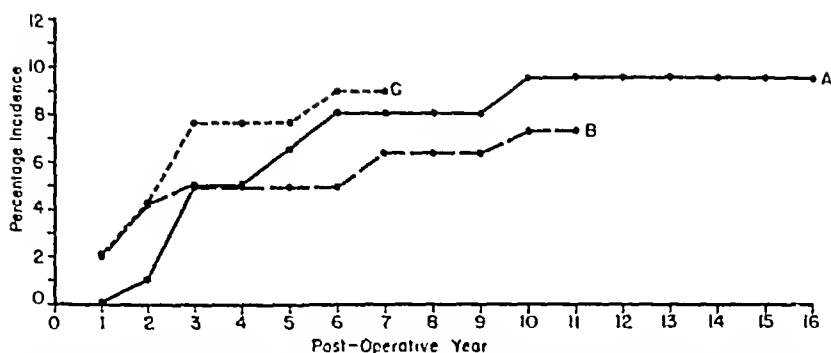


Fig. 4 Median trend curves for the cumulative incidence of recurrence of ulceration following subtotal gastrectomy for duodenal ulcer: A, Surgical years, 1923-1925; B, 1926-1930; C, 1931-1934

low up must be adopted for the study and no patient who has been followed for less than this minimum period may be included in the corresponding population sample. Of course, if the total number of cases is large enough and the period of observation long enough, the entire group of cases may be split into two or more subgroups of different limiting durations, and these can be analyzed independently of each other. (4) The measure of failure is calculated in three ways: (a) the *minimum possible incidence*, based on the total number of operative survivors which might potentially have been followed for the indicated postoperative time, (b) the *maximum possible incidence*, based on the total number of cases which actually were followed in the course of the indicated postoperative year, and (c) the *median incidence*, which is an average of the maximum and minimum possibilities. (5) The year-by-year cumulative trend curve for the (median) measure of incidence is studied with a view to establishing a patient's chances of recurrence at any time following operation. (6) Finally, from such a trend curve, it is possible to set up an *index of failure* of the operation in question. This is given by the median percentage incidence of recurrence at the plateau, and it represents the maximum chance of recurrence, irrespective of time, to be expected for the conditions which characterize the group of cases under analysis.

Such an *index of failure* constitutes a statistical measure of the efficacy of the operation. It is a single number which represents the en-

tire mass of data in respect to the therapy—in short, a “statistic.” This commits us to a statistic which measures “failure” rather than “success”, although the two appear to be complementary they are not entirely so, for an unsuccessful case always remains unsuccessful, but a successful one may become a failure at any time. Studies involving the index of failure are subject to breakdowns according to different variables (age, acidity, obstruction, etc.), and appropriate tests of statistical significance must be applied in these situations wherever they are required. In the consideration of any new candidate for surgery, it must be remembered that his risk of recurrence may be influenced by the special characteristics which his case presents, and that the various factors which may contribute to the recurrence of the disease are of the utmost importance in this regard. Such breakdowns of the data are not illustrated here, but they will be presented in a subsequent report on an actual experience at this hospital.

In searching the literature dealing with the end-results of ulcer therapy, we were impressed by the fact that in years past almost no attention was given to the basic problems of statistical methodology. The first such study to indicate an awareness of these problems was published by St. John (3) in 1930 and this was followed 9 years later by a detailed development of his earlier ideas (4). Apart from the contributions of this group of workers we know of no other publications which manifest any consciousness of the com-



plexity of the biometrical problem facing the clinical investigator of ulcer therapy. A recent paper by Campbell called the attention of the surgical profession to the problem of random sampling as it applies to the interpretation of postoperative mortality data in general, and it emphasized the importance of tests of significance in the comparison of "percentages" based on different groups of cases—but it gave no consideration to the statistical evaluation of therapeutic end result. When we first set out to develop a statistical technique for our own use we were concerned with discovering the ultimate success or failure of an operation for peptic ulcer and *how long we must continue to observe our cases after operation in order to determine this factor*. In scrutinizing the procedures previously followed for determining the end results of treatment we could find none which afforded this information to our satisfaction. Thus, the use of an *average period of follow-up* for a group of patients may lead to a numerically different picture from that which would be obtained if every individual in the group had been studied for the same length of time. Furthermore the use of any arbitrarily limited period of observation to establish a measure of therapeutic success (e.g. a 5 year follow up period) cannot be accepted until it has been validated by an independent statistical study of its merits, and we were aware of no such study. Hence we were under the necessity of devising a statistical procedure which would fulfill the requirements of this problem as we perceived them. The result is the method described in this report.

Let us consider the limitations of this new statistical method. Some of these limitations are inherent in any statistical procedure for the study of therapeutic results especially of a disease like peptic ulcer—others may be specific to the present method alone and these should be clearly recognized.

1. The reliability of the raw data (i.e. of the characteristics of the clinical material chosen for analysis) is always open to question. Apart from the personal equation of the investigator the descriptive nature of the phenomena sometimes makes a clear-cut classification impossible. For instance a case of painless bleeding following subtotal gastrec-

tomy may result from a recurrent ulcer, an erosion or an inflammatory disorder, gastritis or jejunitis. The interpretation of such a case therefore must always be open to some uncertainty.

2. The loss of follow up material may prove to be a serious handicap to any statistical study related to peptic ulcer. To cope with this problem it is necessary first of all that every effort be made to develop a follow up organization of the utmost efficiency. This requires a specialized personnel, dedicated to the task of tracing a patient by every possible means. Concerning the residue of unfollowed cases, one may assume that their results on an average are or are not essentially different from those for the cases actually observed. If one or the other of these assumptions must be made in order to carry on with the statistical study. Limiting the study to the cases actually observed and disregarding the unfollowed cases involve the tacit assumption that the latter are statistically homogeneous with the followed group. Some clinicians may prefer to perform no statistical studies but ever rather than commit themselves to any such assumption. We feel that their attitude is unwarranted in that it is purely destructive and contributes nothing to the eventual solution of any problem requiring investigation. On the contrary it is better to perform a study of this kind with all its limitations provided only that the source of the limitations never be lost from sight. A real solution of the problems created by the unfollowed cases can come about in only one way if at all, under present working conditions—that is by means of a central agency to which all clinics must send records of patients who had previously been treated at other institutions. The data so collected should be tabulated according to a generally accepted method and some machinery be established for making the results immediately available to the hospital where each patient was originally treated. After 20 years of inconclusive debate about the results of ulcer therapy this seems to be the most practical solution to the problem presented by the unfollowed cases.

In the absence of such a solution, we have assumed in this particular study that the

followed cases were statistically homogeneous with those which were followed—for reasons which we defined clearly. In addition, however, we set up a dual measure of percentage incidence, in order to minimize any weakness inherent in this assumption. That is, we calculated both maximum and minimum estimates of this incidence, based on the total potential and actual follow-ups of the cases, and we cited reasons for believing that the true value lies between these two extremes. For convenience, in comparing different groups of data, we have employed the median average of these two limiting values as the most probable index of failure.

3. Assuming that neither of the foregoing limitations offers a serious obstacle to a statistical investigation, we next are confronted with the following question: Given 2 independent sets of observations or results by the same operation, which yield manifestly different total incidences of recurrence, how can we be sure that their difference is significant according to the usual statistical criteria? Before any consideration is given to possible reasons for a difference in results between two sets of data (such as surgical technique, or racial and economic characteristics of the patients), it must be established that the difference cannot be due solely to random sampling—in other words, that the difference is larger than is likely to occur between 2 groups of cases drawn from a single large uniform population. For this purpose we have employed the accepted statistical technique of a significance test based on the ratio of a difference between 2 means (or percentages) to its own standard deviation—sometimes called the *significance ratio* (See Appendix). If the data in question be subjected to this type of statistical analysis and it develops that the difference is *not significant*, then it follows that the difference between the 2 sets of data, *in all probability*, is a result only of the accidental variation in biological material which arises in the choosing of sample groups from a large parent population. In the several population samples used here to illustrate our technique, the differences both for 5 year and for 10 year follow-ups clearly had no statistical significance. On the other hand, had the difference in these

incidences of recurrence proved to be significant, then it would be incumbent upon us to seek the factors responsible for the dissimilarities.

Clinical investigators are generally unaware of (or indifferent to) the concept of *random sampling*, and the errors which may result from its neglect. This statistical concept is simple and requires no special mathematical knowledge for its comprehension. Let us assume, for instance, that there exists a recurrence index which truly characterizes the surgical procedure under discussion, as it might be applied in *all* cases—past, present, and future. Such a group of cases constitutes a theoretical “universal population” of all cases subjected to this operation. If, now, we choose “samples” of this “universe” (i.e., small groups of the cases which constitute the universal population) we will find that the recurrence index for any such sample may differ materially from that for the other samples as well as from that for the entire population. If any such smaller group of cases is chosen entirely at random, so that no major factor differentiates it from any other sample of the universal population, then the differences among these several indices may be expected to conform to certain statistical laws. If the difference between any two such indices is greater than may be expected from these mathematical relationships, then we say that the two groups of cases are significantly different in that some factor or group of factors is present in one situation and absent from the other. Such use of these mathematical relations constitutes the test of significance of a difference between 2 groups of data, already referred to. It must be noted that 2 samples from the same population may differ materially in their recurrence index, but their difference may not be significant in the statistical sense. This being the case, the clinician must be very wary about drawing conclusions from such comparisons, unless he is quite certain that the difference has not arisen purely by reason of random sampling. Note also that the result of a significance test may be indecisive, in that it fails to indicate clearly that the difference between two values is, or is not, significant. This may happen because of the size of the

difference relative to its standard deviation, i. e. the probability ratio lies between 1 and 2.6 (see Appendix).

4. In connection with the preceding there arises a question concerning the number of cases in each set of data and their adequacy for such a comparison. If the difference between the percentage incidences for 2 groups of cases is clearly significant (or not significant) with a high degree of probability, then the number of cases may be considered adequate even when the group is as small as 15. If on the other hand the difference is of indecisive significance increasing the sizes of the samples may serve to eliminate the uncertainty on this score. Clinicians frequently ask this question in another form "Having conducted a study on a single group of cases and having arrived at an index of mortality or of operative success how can one be sure that the number of cases in the group is sufficient for drawing valid inferences? But what do clinical investigators expect from their studies in the way of 'inferences'? Such expectations are twofold (a) an evaluation of their therapeutic results relative to a second set of data—in other words a comparison of 2 groups of results (b) a measure of such efficacy as may be expected for a similar group of data not yet treated—in other words, prediction of the degree of success which may be anticipated in the future on the basis of an adequate past experience or trial sample.

For the first of these expectations one can say that if the test for significance of the difference between the 2 sets of data is clearly decisive with a high degree of probability (taking suitable account of small number theory) then the number of cases is satisfactory. We have previously referred to the use of the *standard deviation* of a mean value or a percentage as the basis for tests of statistical significance. The magnitude of this statistical criterion of scatter of a group of data is determined by the size of the sample population as well as by the mean or percentage incidence value itself. Hence if we are concerned with the therapeutic indices of 2 sets of data, and we desire to know whether these sets contain a sufficient number of cases for the purpose of comparing them we must first apply the sig-

nificance test to the difference between the 2 indices. If the result be clearly decisive either for significance or for non-significance then we may say that the number of cases is probably adequate for the purpose in hand. If however the result proves to be indecisive, then we are under the necessity of gathering more data before any conclusion can be drawn. The resultant increase in the total number of cases will in general decrease the standard deviation of the mean or percentage and thereby increase the likelihood of our arriving at a decisive conclusion from the test for statistical significance.

The second of these expectations (prediction) presents a more difficult problem. It is obvious that the larger the trial sample the more reliable will be the statistical inference drawn from it. Nevertheless, under certain circumstances even samples as small as 15 cases may afford a basis for prediction of considerable validity. Whether this number is adequate however can be learned only after several such trial groups have been compared in order to learn something about the variation from sample to sample. Furthermore it must be remembered that prediction is always fraught with uncertainty because it presumes that the general characteristics of the group of cases for which prediction is being made do not differ significantly from those of the trial groups on which the therapeutic index is determined—in other words, that they are all random samples of the same universal population. Without this homogeneity it is obvious, results on the one group cannot be predicted from those on the other. Granted the comparability of the 2 groups however we may then expect that the index of our predicted group will agree with that for the trial group only as well as any 2 trial groups will agree with each other. We must not lose sight of the uncertainties arising from random sampling and we must remember that a future result may differ from a predicted one by as much as the laws of chance or random sampling allow for. Hence the investigator must learn that clinically identical material may yet differ in regard to surgical or therapeutic results by considerable amounts. For practical purposes, he is under the necessity of

making such predictions for the guidance of himself and his colleagues, but he must be constantly aware of the possibility that his prediction may fall down. In other words, he is taking chances in the statistical as well as the vulgar sense.

What can we say about the number of cases required to establish a valid index for a group of data, without reference to any other group—past, present or future. The consideration of any isolated group of cases in this way is always valid, irrespective of the number of cases, *provided that the index so calculated is accepted only to describe this one group of cases.* This means that the clinician does not intend to use this index as a reflection of any other clinical experience whatsoever, but only for the purpose of description, and here the question of statistical validity does not ordinarily enter. However, just as soon as the index for this group be compared with that for another experience, or be used for predicting the risk or chances of success in a group of cases about to be treated, then we are confronted with a wholly different situation—one in which the process of inference and the question of statistical validity must always be uppermost in the mind of the investigator.

#### SUMMARY

This report is introduced with a review of the procedures which have been employed by clinical investigators for evaluating the results of their therapeutic (chiefly surgical) methods for peptic ulcer. Following a discussion of the statistical weaknesses of these procedures and of certain fundamental conditions which must be adhered to in order to insure statistical validity to any such procedure, we have presented a statistical procedure of our own which conforms to these requirements. For this purpose, and in order to cope with the problem arising from unfollowed cases, we have adopted the following premise: that the incidence of failure among the group of unfollowed patients is no greater than among the observed group, and it may be even less. We believe that this premise is valid for ulcer surgery with a high degree of probability, but if future evidence necessitates its modification we are prepared to change it according to the facts.

The new method yields maximum and minimum estimates of the cumulative trend curve (by years) for the percentage incidence of post-therapeutic recurrence of ulceration. From such a pair of graphs, we calculate a median average curve which we believe to have greater validity than either of the limiting curves. In order to facilitate description of this statistical technique we have employed 3 sets of data from the records of the Mount Sinai Hospital, for cases of duodenal ulcer which had been subjected to subtotal gastrectomy during the years 1923–1934. The statistical concept of random variation is discussed, particularly in relation to the variations among these 3 series of cases and to the number of patients which may be considered adequate for such a study. The several median trend curves give evidence for the existence of a plateau beyond the 10th year—which means that, in all likelihood, any patient operated upon will develop a recurrence either during the first 10 postoperative years or not at all. From these data, the average total incidence of recurrence following subtotal gastrectomy for duodenal ulcer is in the neighborhood of 9 per cent.

Although various therapeutic measures have been devised to control or abate ulcer activity, none can assure a certain cure of the disease. Moreover, since the results with these therapies may be influenced by a multiplicity of factors, the quantitative measurement of their efficacies resolves itself into a statistical problem. This implies the use of a logical, well conceived technique, which fulfills the requirements of statistical theory. The failure to recognize this basic idea of methodology has contributed in a large measure to the confusion, which has now existed for more than two decades, concerning the results with certain surgical therapies for peptic ulcer. Unless the basic importance of "statistical methodology" is recognized, there is no reason to expect future efforts in this problem to be any more conclusive than those of the past.

A detailed discussion of these data from the clinical point of view, including the characteristics of the material, the factors which influence the results of operation at this hospital, and the implication of our statistical conclusions, will be presented in a later report.

## REFERENCES

- CAMPBELL, H. E. *Surgery* 94 9 25.  
 HILL, A. B. *Principles of Medical Statistics*. 2d ed.  
 London: The Lancet Limited, 1939.  
 3. S. JONES, F. B. *Ann Surg* 93, 92 397.  
 4. S. JONES, F. B. HARVEY H. D. GILES, J. A. and  
 GORDON, T. E. *Ann Surg* 93, 99 93.  
 5. YULE, G. U. and KIDMAN, J. G. *An Introduction to  
 the Theory of Statistics*. 11th ed. London: C. Griffin  
 and Co. Ltd. 1937.

## APPENDIX

The significance test used in this report is the elementary one based on the "probability ratio." For this particular situation let

$p$  = the fractional percentage incidence of recurrence (in say sample A (i.e., the percentage incident divided by 100))

$p_1$  = the corresponding value for sample B

$n$  = the number of cases in sample A which is taken as the mean of the original number of operative survivors and the number of patients seen at follow-up in the tenth year

$n_1$  = the corresponding value for sample B

Then  $p_1 - p$  = the difference in fractional incidence of recurrence between the two samples (i.e., the value whose significance is to be tested)

$s_1$  = the standard deviation of  $p_1 = \sqrt{\frac{p_1(1-p_1)}{n_1}}$

$s_2$  = the standard deviation of  $p = \sqrt{\frac{p(1-p)}{n}}$

and the probability ratio is given by

$$PR = \frac{(p_1 - p)^2}{\frac{s_1^2}{n_1} + \frac{s_2^2}{n}}$$

If  $PR=1$  it means that the difference ( $p_1 - p$ ) may be the result of random sampling 317 times in every 1000 experiments, and therefore that it is significant of some particular influence other than random sampling 68 times in every 1000. If  $PR=2$  the chances that the difference is significant are 95 in 1000 and if  $PR=3$  the probability of significance is around 997 in 1000. In order for the probability of significance to be 99 in 1000 or 99 per cent  $PR$  must be 3.6. The latter value for  $PR$  is the one accepted as critical in the present investigation. If any pair of percentage recurrence values yield a  $PR$  value of 3.6 or greater the difference between them is said to be significant at the 1 per cent level of probability. Nonsignificance is indicated by  $PR=1$  or less and a value between 1 and 3.6 may be considered indecisive. There is available a more refined procedure based on the estimation of the standard deviation of the parent population from which samples A and B are supposed to have been drawn but such refinement is hardly warranted for our present purpose.

The following table contains a summary of the several significance tests referred to in the text. The subscripts indicate the duration of follow up in each case.

Samples	$p_1 - p$	$N$	$\chi^2$	$PR$	$\frac{p_1 - p}{s_1}$
$A_{10}$ and $B_{10}$	$0.04 - 0.07 = .03$	71	1.23	1.6	1.0
$A_5$ and $B_5$	$0.07 - 0.09 = .02$	77	1.08	1.5	1.0
$C_5$ and $B_5$	$0.07 - 0.08 = .01$	86	.66	.8	1.0
$C_5$ and $A_5$	$0.07 - 0.05 = .02$	86	.77	.9	1.0

# THE EFFECT OF THORACIC DUCT DRAINAGE AND HEMORRHAGE ON THE BLOOD AND LYMPH

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A MPLE investigation has been made of the changes in the blood caused by the redistribution of fluid and protein in the acute phase of hemorrhage. Recent advances in the physiology of hemorrhage resulted in the suggestion by some observers (3, 4) that the lymph might be an important factor for the replacement in the blood of essential elements lost by bleeding. However, no direct studies on both the blood and lymph have been reported since Haynes's observation on the concentration of proteins in blood and peripherallymph during hemorrhage.

In the present investigation, the effect on the specific gravity of the blood and lymph, of acute hemorrhage, of continuous lymph drainage, and of both acute hemorrhage and continuous lymph drainage was studied.

The animals were divided into 3 groups and were prepared in the following manner. Dogs whose average weight ranged from 13 to 16 kilograms were anesthetized by an intravenous injection of 1 cubic centimeter of 3 per cent pentobarbital-sodium per kilogram of body weight. Endotracheal artificial respiration was administered by a differential insufflation machine. Kymographic tracings of arterial pressure were taken from the femoral artery.

The dogs of group I were subjected to drainage of lymph by cannulation of the thoracic duct which was exposed in the neck and disconnected from the subclavian vein at their point of junction. The lymph was drained continuously and collected in citrated tubes at 20 minute intervals for a period of 3 hours. In addition also at 20 minute intervals, 45 cubic centimeters of blood was drawn from the

femoral artery. The dogs of groups II and III served as controls. The animals of group II were subjected only to repeated bleedings and consisted of the withdrawal of 45 centimeters of blood at 20 minute intervals. The third group of animals was subjected to the continuous drainage of lymph without hemorrhage.

The following determinations were made. The specific gravity of the blood, the plasma, and the lymph was determined by the falling drop method of Barbour and Hamilton (8). The hematocrit cell volume was measured in Wintrobe tubes. The changes in the density of the lymph, the blood, and the hematocrit values after the injection of nembutal were regarded as the initial values in contradistinction to the normal preanesthetic values.

## RESULTS

*Group I Rapid progressive hemorrhage and continuous lymph drainage.* Ten dogs, each with an approximate weight of 16 kilograms, were subjected to an average loss of 21 per cent of their total blood volume and a loss of lymph equivalent to 18 per cent of the total amount of blood withdrawn.

Lymph obtained by continuous drainage during the experimental period averaged 89 cubic centimeters. The smallest amount obtained was 58 cubic centimeters, the greatest 120 cubic centimeters. In 7 dogs, the specific gravity of the lymph increased progressively over its initial value (1.0187, average) during the course of the repeated bleedings. The increase averaged 0.0057, so that in some cases, the final specific gravity of the plasma and lymph was almost equal. In the 3 other dogs, the specific gravity of the lymph fell below its initial value. The fall averaged 0.0018.

The specific gravity of the plasma tended to decrease progressively, but for the exception of one or two small increases which corresponded to similar changes in the density of the

From the Laboratory of Experimental Surgery Department of Surgery, New York University College of Medicine.  
Aided by a grant from the New York Foundation.  
Prepared for presentation before the Forum on Fundamental Surgical Problems, 1942 Clinical Congress of the American College of Surgeons, which was cancelled because of the war.  
Dr Shafiroff now Major M.C., A.U.S. Dr Doublet now Captain M.C., A.U.S., Dr Preiss now First Lieutenant M.C. U.S.A.R.

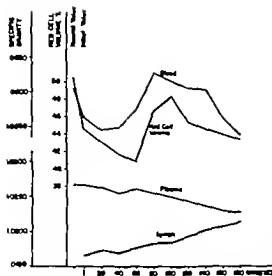


FIG. 2. Changes in the blood and lymph during rapid hemorrhage and continuous thoracic duct drainage. Group I, experiment 2. The initial specific gravity of the blood is markedly reduced below the normal value as a result of the injection of nembutal (engorgement of the spleen). After the first bleeding, there is a further small decline in specific gravity of the blood. After the third bleeding, the specific gravity of the blood increased above its normal value (contraction of the spleen). Thereafter, with subsequent bleedings, the specific gravity of the blood fell almost progressively. The changes in the hematocrit show parallel those of the blood. The specific gravity of the plasma declined progressively except for brief periods when it increased slightly coincident with the increase in the specific gravity of the blood. The specific gravity of the lymph increased markedly and almost equalled the specific gravity of the plasma.

whole blood. The initial specific gravity of the plasma was 1.0275 (average) and its maximum fall was 0.0063 (average).

The specific gravity of the whole blood at the end of the experiment fell 0.0026 (average) below its initial value (1.0553 average). The decline in specific gravity of the whole blood was usually progressive for the first three bleedings and was followed by a temporary sharp increase in density after which there was a continuous fall in specific gravity until the end of the experiment.

Corresponding with the increase in the specific gravity of the blood the hematocrit values (39.5 volumes per cent average initial value) also increased 5.3 volumes per cent (average). At the end of the experiment the hematocrit cell volume was reduced 8 volumes per cent (average) below its initial value.

The initial blood pressure (123 mm. Hg. average) fell approximately 4 millimeters mercury with each bleeding and recovery usually took place within 5 minutes. After the sixth withdrawal of blood, the arterial pressure fell to 80 millimeters mercury (average) and recovery to the latter level in the subsequent bleedings required about 12 minutes. In 4 of the dogs from whom the greatest amount of lymph was obtained by drainage, the blood pressure fell to 20 millimeters mercury (average) after the sixth bleeding. In the others, the blood pressure varied from 65 to 76 millimeters mercury.

*Group II Hemorrhage experiments in intact animals.* Ten dogs with an average weight of 18 kilograms were subjected to a loss of 24 per cent of their total blood volume by repeated bleedings.

The specific gravity of the plasma (1.061 average) fell 0.0038 (average) as a result of the bleedings. The specific gravity of the whole blood (1.0595 average) and the hematocrit cell volume (39.7 volumes per cent average) as in the previous group, increased for a brief period and then fell progressively to 1.0552 and 36.3 volumes per cent (average) at the end of the experiment. The initial blood pressure approximately 118 millimeters mercury (average) declined with each withdrawal of blood. Recovery of blood pressure was similar in character to the recovery change in the previous group and at the end of the experiment ranged between 70 to 76 millimeters mercury.

*Group III The effect of continuous lymph drainage on the blood.* Five dogs with an average weight of 15.8 kilograms were subjected to continuous thoracic duct drainage as a result of which an average of 93 cubic centimeters of lymph was obtained from each animal. At 20 minute intervals, 5 cubic centimeters of blood was drawn to determine changes in the hematocrit cell volume and in the density of the blood. In this way only 0.03 per cent of the blood volume was lost. The initial specific gravity of the lymph averaged 1.0198 and all determinations varied no more than 0.0011 from this value. The specific gravity of the whole blood (1.0579 average) varied 0.0012 above or below the initial value while that of the plasma (1.0291 average) likewise varied 0.





lymph flow from the thoracic duct were estimated at 31 cubic centimeters per hour there could be a maintained return to the blood by this route of approximately 1 to 2.5 grams of protein per hour. Thus a loss of 27 grams of protein as contained in 360 cubic centimeters of blood might be restored within 27 hours by this lymphatic channel. Since the loss of protein and fluid by continuous lymph drainage alone was small it was plain why this did not markedly affect the specific gravity of the blood or plasma, while hemorrhage combined with lymphaticostomy was effective in changing significantly the density of the blood and resulted even in the precipitation of shock in some cases.

The other phases of hemorrhage involving changes in blood pressure, hematocrit cell volume, blood and plasma specific gravity have been adequately investigated by Schlomberg and Sawyer and Adolph *et al.* (2) and reaffirmed in this study. Reductions in blood volume of less than 30 per cent, as in these experiments, did not impair the activity and response of the sympathetic nervous system which maintained blood pressure above shock levels and thus influenced the transfer of tissue fluids to the blood in accordance with the Starling concept. The changes in hematocrit cell volume and whole blood specific gravity have already been shown to be due to engorgement of the spleen in association with the anesthetic agent (1) after which followed a rapid emptying of the spleen mediated by the sympathetic nervous system and activated by the process of hemorrhage. Plasma dilution

in hemorrhage is now a well recognized fact which has been demonstrated by many observers (3).

#### SUMMARY

The effect of hemorrhage on the blood and lymph was partitioned and studied. It was found that coincident with blood plasma dilution there was usually a concentration of the density of the lymph in dogs subjected to both the loss of blood and lymph. In the animals without lymphaticostomy the changes in the specific gravity of the blood and plasma during the bleedings were not as marked as in the previous group. Continuous lymph drainage for a 3 hour period without hemorrhage failed to affect significantly the specific gravity of the blood.

The lymph served an important rôle in the compensatory mechanism of hemorrhage not only as a pathway for fluid but also as a source of protein replacement.

#### REFERENCES

- ADOLPH, E. F. and GRUBER, M. J. *Am. J. Physiol.*, 933, 66, 95.
- ADOLPH, E. F., GRUBER, M. J. and LEROUX, V. J. *Am. J. Physiol.*, 933, 64, 502.
- CALVIN, D. B. *J. Lab. Clin. Med.*, 41, 26, 44.
- DEWEES, C. K. Quoted by Cahill, New Orleans lecture.
- DEWEES, C. K. and JOFFEY, J. M. *Lymphatics, Lymph, and Lymphoid Tissue*. Cambridge, Mass. The Harvard Press, 94.
- PIPER, F. W. *Am. J. Physiol.*, 91, 104, 5.
- SCHLOMBERG, T. and SAWYER, M. L. *Am. J. Physiol.*, 913, 64, 95.
- SCUDGER, J. *Shock*. Philadelphia, J. B. Lippincott Co., 940.
- SULLIVAN, F. H. *J. Physiol.*, 944, 6, 24.



in which there was any evidence of a fracture infection trauma, or whose roentgenograms were not technically satisfactory. It was our opinion that any narrowing occurring in this age group must be of congenital origin since destructive changes incident to trauma would be less likely encountered in children. Review of these x-ray films disclosed three cases, Figures 13 and 14 of narrowing other than that resulting from such obvious pathological processes as tuberculosis sclerosis, osteochondritis or osteomyelitis. Roentgenograms of these cases revealed associated anomalies, lumbarization or sacralization being present in all instances. Williams also examined a like number of films and found only one which had a narrowing which could be considered congenital in origin. Williams states, however that there is one type of congenital spine which presents a sacralization of the 5th lumbar vertebra. The lumbosacral disc in such a case shows the narrow character of the sacral intervertebral disc. Confusion may arise when there is partial lumbarization of the first sacral segment. The intervertebral disc between the 1st and 2nd sacral vertebrae retains its narrow character and from a lateral view may be mistaken for the lumbosacral disc. Willis emphasized this observation in saying "Still a third manifestation of partial sacralization of a last lumbar segment and one that is often wrongly interpreted as a pathological lesion is narrowing of the lumbosacral disc. In anomalous sacralization the vertical diameter of the disc may vary between the usual thick lumbosacral type and that of the thin sacral disc. A thin disc is in itself no part whatever of a destructive or pathological lesion. Particularly if such a disc is associated with enlarged transverse processes or other evidence of anomalous sacralization as are most of these shown in clinical discussions such pathological interpretation must be received with considerable reservation. Hodges and Peck have written "The finding of a narrow disc is undoubtedly to be expected in the case of patients showing evidence of bilateral or even unilateral fusion of the 5th lumbar vertebra with the sacral mass."

Our small series is essentially in agreement with the findings of others that such congenital narrowing exists only in the presence

of other structural anomalies at the lower point of the spine. It would seem then, that a narrowing of the lumbosacral disc as a congenital anomaly exists frequently enough to be of diagnostic significance.

In a short period of time we have seen x-ray films of several adults whose lumbosacral space has been appreciably narrowed. These were cases of low back pain without sciatica, whose history and findings were not suggestive of a ruptured disc.

#### CASE REPORTS

**CASE 1.** M. H. White female aged 31 years, was first seen in out-patient dispensary complaining of pain over the low back and coccyx of 6 weeks duration. The onset of pain dated from a recent fall out of a swing, the patient landing on her buttocks. Her greatest pain was localized over the coccyx and lower sacrum and at no time had there been any radiation of pain down either leg or onto the abdomen. Rectal examination revealed the coccyx to be normal in contour and without angulation, but movement of the coccyx between the examining fingers produced exquisite pain. Examination of the low back revealed normal range of motion without muscle spasm or tenderness. Leg signs were normal, knee and ankle reflexes were intact, and there were no sensory or motor changes in either extremity. The diagnosis was tear of the sacrococcygeal ligaments. She was placed upon six baths and local heat under which she made satisfactory response. X-ray films (Fig. 1 and 2) taken of the lumbosacral region, revealed an appreciable narrowed interspace at lumbosacral junction with lumbarization of 1st sacral vertebra.

**CASE 2.** W. E. negro male aged 27 years, was seen in the out-patient dispensary because of low back pain of 6 months duration. He ascribed the onset of the pain to lifting of some heavy rocks at that time. There was no history of radiation of pain down either leg or onto the abdomen. Examination of the low back revealed marked muscle spasm of the erector spinae on both sides at the lumbar level. There was an exaggeration of the normal lumbar lordosis. All back motions were sharply restricted. There was generalized tenderness over the zygapophyseal joints bilaterally at the lower lumbar levels and over the sacrum. Straight leg raising was limited to 170 degrees on both sides. Babinski, ankle and knee reflexes were equal and normal. The diagnosis of irremediable tear of the extensor musculature was made. Adhesive tape strapping followed by low back support afforded complete relief in 3 weeks. X-ray films (Figs. 3 and 4) revealed transitional type of lumbosacral spine of the 1st sacral segment and large transverse processes of 5th lumbar which articulated with the alium. The intervertebral space between the 5th lumbar and 1st sacral narrowed by 10 to 15 per cent.





Figs. 1 and 2. Type of transitional lumbosacral junction which is less likely to be confusing since the lumbosacralization of the 1st sacral is so obvious. This is the only case in which an acute lumbosacral angle was noted.

that the pain was aggravated by weather changes. There was radiation of pain down the posterior aspect of the right thigh and lateral aspect of the calf to the level of the ankle. His back pain was worse on lifting. Coughing and sneezing had no effect. There was no paresthesias in the right leg. Examination revealed moderate muscle spasm of both sides of the lumbar level. All back motions were excellent and there was a minimal amount of tenderness over the zygapophyseal joints over the lower lumbar levels on both sides. Leg signs were normal. Knee, ankle, and Babinski reflexes were negative and there were no motor or sensory changes in either leg. Roentgenograms (Figs. 3 and 4) revealed healing transverse fracture of the body of the sacrum with arthritic changes of the articular facets at the level between the 5th lumbar and 1st sacral. In addition there was partial sacralization of the 5th lumbar vertebra with the lumbosacral intervertebral disc of the usual intermediate character.



Figs. 3 and 4. Transitional type of 5th lumbar vertebra in child. The interspace between the 5th lumbar and 1st sacral still persists into maturity in its narrowed character.



Figs. 5 and 6. This type is difficult to recognize and symptoms suggest herniation of the intervertebral disc. The true character of the 5th lumbar best appreciated from the anteroposterior view.

CASE 5. M. C., negro, aged 52 years, was first seen at the orthopedic dispensary in June 1922, because of pain in the low back radiating down the posterior aspect of the right leg. He had had multiple gonorrheal joints, which were diagnosed by smear and culture, secondary to chronic pyelonephritis. In October 1921 she began to develop pain over the right buttock, which radiated down the leg. In May 1922, she experienced recurrence of pain in the shoulder and elbow. She stated that sneezing and coughing gave her leg pain as did lifting. The patient had had syphilis many years before for which he had received inadequate therapy. Examination revealed tenderness at the lumbosacral junction in the midline. All back motions were normal. There was about 10 degrees limitation of straight leg raising on the left. The ankle jerks were equal but the left knee jerk as absent. Babinski as normal and sensory examination was negative. X-ray films of the lumbosacral junction (Figs. 5 and 6) revealed moderately severe spondylorhithitis and spondylitis. In addition there was a lumbosacralization of the 1st sacral segment with an acute lumbosacral angle. The diagnosis was traumatic arthritis secondary to asymmetrical, mechanically poor lumbosacral junction on congenital basis.

CASE 6. A. J. negro female aged 36 years seen in the orthopedic out-patient dispensary. In May 1922 when she complained of sudden onset of low back pain of 6 weeks duration. There was no history of trauma and her low back pain was constant with radiation down the lateral aspect of both thighs as far as the knee. Stooping was impossible because of pain. Examination revealed exaggeration of the normal lumbar lordosis with considerable limitation of all low back movements due to muscle spasm. There was tenderness at the lumbosacral level to the midline. Straight leg raising up to 90 degrees on both sides. Neurological examination was negative. The impression was low back strain aggravated by obesity. X-ray film (Figs. 7 and 8) revealed lumbosacralization of the 1st sacral

their skins. Since the cornified layer of the rabbit's epithelium is thin and is of little protective value against tannic acid, the tannic solution penetrated deeply to destroy the entire epithelium. Taylor also studied a biopsy taken from a human burn which had been treated by tannic acid. His observations led him to suggest that tannic acid may damage normal structures.

Amegrostidis has made the most complete study of tissue reactions to medicants applied in the treatment of burns. He produced burns on rabbits by hot water and hot irons with destruction of the epithelium and a portion of the corium. Various medicants were applied to the burns including tannic acid solution, tannic acid plus silver nitrate, fish muth dressings, and cod liver oil ointment. Some of the experimental burns were completely covered either by dressings or by eschar, and the prepared sections were stained by appropriate methods. Upon examination of the biopsy specimens Amegrostidis found the medicants deposited in irregular clumps on the surface and portions within the eschar. He also found that some of the materials had penetrated the epithelial cells and the corium. In the biopsy specimens taken at 10 days the necrotic layer had separated from the viable remaining dermis which had become completely re-epithelialized from the edge of the burn. Amegrostidis presented the startling conclusion that all the experimental burns healed with equal rapidity regardless of the treatment applied. Furthermore, he was unable to find any histological differences in the treated and the untreated lesions.

In some of the studies mentioned it has been suggested that the coagulating action of tannic acid produces damage to normal structures. If this hypothesis be correct, tanning agents applied to superficial burns may produce further damage by destroying the basal layer of the epithelium and the glands of the corium, which serve as sources of regenerating epithelium. It would seem important to know the effects of various medicants on normal tissues if these materials are to be applied to tissues damaged by burns. Since a thorough knowledge of the effect of tanning agents and of vaseline gauze on normal and burned tissues



Fig. 1. Corium of biopsy specimen from donor site in rat taken after removal of graft with dermatome. (85

is not available, we decided to investigate the problem.

#### MATERIALS AND METHODS

The ideal way to study the effect of tannic acid on the tissues beneath burned epithelium would be to take biopsy specimens of the burn before the application of tannic acid and at suitable intervals after. There are, however, certain difficulties in applying such a procedure to humans. Furthermore, accidental burns are not of uniform depth and one has no guarantee that several specimens removed from a burn will be from areas of equal tissue destruction. This is true even though the specimens be taken within a half inch of each other. In order to determine how much of the destruction is due to tannic acid, it is necessary to begin with a burn of constant depth. It is not possible with humans to obtain an accidental burn of constant depth, but it is possible to obtain a skin injury of constant depth through use of the Padgett dermatome. This machine, originally developed by Padgett for the purpose of cutting Thiersch and split thickness grafts, enables one to remove a uniform layer of skin of almost any desired thickness. When a layer of skin is removed by means of a dermatome, the knife usually removes the epithelium completely plus a narrow portion of the papillary layer of the corium. The hair follicles, the sweat glands, and the sebaceous glands in the remaining corium are left unharmed (Fig. 1). These structures will serve as the source of

# A COMPARISON OF THE EFFECTS OF TANNING AGENTS AND OF VASELINE GAUZE ON FRESH WOUNDS OF MAN

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CERTAIN criticisms have recently been made of the tannic acid method of treating burns. Although the use of tannic acid for the treatment of burns has been widely adopted, some surgeons have found that burns covered with vaseline impregnated gauze heal more rapidly than comparable burns treated with tannic acid. Since there are numerous conflicting opinions regarding the efficacy of various types of burn therapy we decided to compare the tissue alterations due to tanning agents with the tissue alterations found following the application of vaseline gauze.

Davidson introduced the tannic acid method of burn treatment in 1915 because of his belief that burned tissue liberated substances responsible for the so called "burn toxemia." Since "tannic acid forms a more or less stable compound with the protein constituents of body fluids and cells," he hoped that it would precipitate the poisonous materials in burned tissue and thereby prevent their absorption." Davidson was aware that tannic acid especially in high concentration, might have a possible deep caustic action, and therefore he advocated that it be applied as a 2½ per cent solution in the form of wet compresses. Furthermore the burns were to be inspected at 12, 18 and 24 hours for evidence of tanning and as soon as the surface assumed a light brown color the application of tannic acid was to be discontinued.

There have been many modifications in the method of applying tannic acid. Perhaps the most important of these is that of Bettman in which a single application of 5 per cent tannic acid is followed by a single application of 10 per cent silver nitrate. Bettman claims that

this method is superior to tannic acid alone because it produces a thin flexible eschar—and thus almost instantaneously instead of over a period of 12 to 24 hours. The introduction of tannic acid revolutionized the treatment of burns, and today probably more burns are treated with tannic acid alone or in combination with silver nitrate than with any other method.

In spite of the wide use of tannic acid there have been comparatively few anatomic studies of the effects of tanning agents on damaged or normal tissues. Lochr and Zacher in 1911, reported their observations on the comparative effects of cod liver oil ointment and of tannic acid applied to burns on domestic pigs. They selected the pig as they believed its skin to be the most suitable for the production of experimental burns. Deep ulcers extending to the subcutis and muscularis were produced by the application of hot soldering irons for ten seconds. Tannic acid or cod liver oil ointment was then applied to the burned areas. The experimenters found that the burns treated with cod liver oil healed more quickly than did those treated with tannic acid. From examination of biopsy specimens of the burned areas obtained at 3 and 6 days, they concluded that the tissues of burns treated by tannic acid appeared to be torporic so that healing was delayed. They noted that an eschar formed when the tannic acid came into contact with the dermis but failed to form when applied to fatty tissues. The histological findings were too incompletely recorded to enable one to judge in detail the reactions of the tissues to the medicament applied.

Taylor in 1936 called attention to the destructive effects of tannic acid which he observed in biopsy specimens taken from rabbits following the application of tannic acid to

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Fig 4



Fig 5



Fig 6



Fig 7

Fig 4 Vaseline gauze treated donor site at 8 hours  $\times 100$

Fig 5 Tannic acid treated donor site at 8 hours  $\times 100$  Note thickness of eschar and leucocyte exudate

Fig 6 Vaseline gauze treated donor site at 24 hours  $\times 100$

Fig 7 Tannic acid treated donor site at 24 hours Note extensive coagulation of dermal collagenous bundles  $\times 100$

*A Comparison of the Effects of Tanning Agents and of Vaseline Gauze on Fresh Wounds of Man*  
—John Winslow Harshfield, Matthew A. Pilling, and Mark L. Munro





Fig. 2. Vaseline gauze treated donor site at 36 hours  $\times 85$ .



Fig. 3. Tannic acid treated donor site at 36 hours  $\times 85$ .

cells which will re-epithelize the surface of the naked dermis. The lesion produced except for the presence of a layer of burned epidermis, simulates a second degree burn. If tannic acid or similar materials are capable of destroying normal tissues their action should be manifest upon their application to such a surface.

A number of opportunities were afforded us to apply tannic acid to such surfaces in patients who were to receive skin grafts. Under spinal or general anesthesia, the skin was washed thoroughly with soap and water. It was then cleansed with 70 per cent alcohol, followed by ether in order to provide a dry surface. The cement which is used in conjunction with the Padgett dermatome was applied, and after it had dried, grafts were cut approximately 0.016 inches in thickness. Bleeding was controlled by pressure with gauze moistened with warm physiological saline solution. As soon as the bleeding was controlled the donor site was sprayed with a freshly prepared solution of 10 per cent tannic acid (pH 3.4). After a few minutes this was followed by a spray of 5 per cent silver nitrate. On the same patient a similar area was prepared as a control. It was covered by a fine mesh gauze impregnated with vaseline. At intervals biopsy specimens for microscopic study were removed under local procaine anesthesia from both donor sites. The specimens obtained were placed in 10 per cent formalin embedded in paraffin and stained with hematoxylin and eosin.

A few patients were treated with a burn jelly containing quebracho tannin 7.5 per cent and meta-di-hydroxy-di-secondary-tert-benzene 1:1000 in a water soluble base. This preparation was used as quebracho tannin has been proposed as a substitute for tannic acid.

The number of times that one can persuade a patient to subject himself to removal of a piece of skin for microscopic examination is limited. However specimens were obtained from a total of 12 patients at irregular intervals up to 10 days, and a complete series of specimens from 1 to 150 hours was obtained from 2 patients. The histological observations recorded here and the photomicrographs presented represent a compilation of all the biopsies studied. Since tannic acid plus silver nitrate and quebracho were found to produce similar tissue changes, the tanning agent used on a specific donor site will not always be specified in the histological observations.

**Observations on patients.** The donor sites which were treated with vaseline gauze without exception healed more rapidly than those treated with the eschar forming substances. In 6 to 14 days re-epithelization was complete in the wounds treated by vaseline gauze while the sites treated with tannic acid and silver nitrate or quebracho burn jelly required from 14 to 21 days for re-epithelization. The patients complained that donor sites treated with tannic acid were more painful than similar sites treated by vaseline gauze and remarked that vaseline gauze alone be used as subsequent graftings.



Fig 4



Fig 5



Fig 6

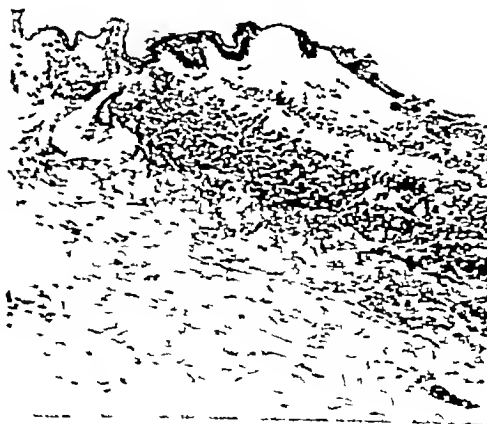


Fig 7

Fig 4. Vaseline gauze treated donor site at 8 hours  
X100

Fig 5 Tannic acid treated donor site at 8 hours  
X100 Note thickness of eschar and leucocytic exudate

Fig 6 Vaseline gauze treated donor site at 24 hours X100

Fig 7 Tannic acid treated donor site at 24 hours  
Note extensive coagulation of dermal collagenous bundles X100

*A Comparison of the Effects of Tanning Agents and of Vaseline Gauze on Fresh Wounds of Man*  
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*Histological observations* At 2 hours wounds treated with vaseline gauze showed a mild exudate of fibrin and red blood corpuscles on the dermal surface with no destruction of collagenous bundles, and as yet no exudate of leucocytes in the area (Fig 2) Biopsy specimens taken from those wounds treated by tannic acid and silver nitrate showed a thick layer of brownish-black material covering the exposed dermis A marked exudate of red blood corpuscles and large clumps of fibrin were found beneath the tanning agents (Fig 3)

Several specimens were available to compare the effects of tannic acid and of vaseline gauze at 8 to 10 hours following their application Donor sites treated with vaseline showed a mild red blood corpuscular and fibrinous exudate with a moderate number of leucocytes in the superficial portions of the dermis and upon its free surface This leucocytic exudate consisted of about equal numbers of neutrophils and mononuclears, the latter being lymphocytes and plasma cells The superficial collagenous bundles showed no abnormalities (Fig 4) Examination of comparable sections treated with tannic acid and silver nitrate revealed the superficial dermal bundles to consist of an acidophilic homogeneous mass covered by the tanning mixture Beneath the eschar granules of the tannic acid could be found at a surprising depth between other collagenous fibers The tannic granules produced considerable variation in the staining qualities of the collagenous fibers, and the edges of some of the bundles stained a deep blue, these changes undoubtedly represent early tissue damage (Fig 5) The more superficial tannic-impregnated homogeneous mass was interrupted by many crevices which widened to produce a separation from the deeper viable dermis In the latter an intense leucocytic exudate was found

Biopsy specimens were taken from only 1 patient 24 hours following treatment of the donor sites Examination of the specimen taken from the wound treated by vaseline gauze showed numerous leucocytes on the surface of the dermis These cells had apparently invaded viable normal staining collagenous tissue A necrotic layer could be

detected upon the most superficial portion of the dermis Inspection of the sweat glands and the hair follicles showed some proliferation of their epithelial cells, this proliferation likely represents an early attempt at epithelization (Fig 6) The donor site treated by tannic acid showed an extensive coagulation of the dermal collagenous bundles, the destruction of the dermis extended many times deeper than the inflammatory exudate seen in the vaseline treated donor site The separating eschar carried with it numerous necrotized sweat glands which would have served as epithelial islands in the repair process (Fig 7)

A number of biopsy specimens were available for examination in the period from 30 to 60 hours following therapy Donor sites treated with vaseline gauze showed an increased inflammatory exudate in and upon the dermis The exudate was chiefly neutrophils embedded in small amounts of fibrin In a few areas there was some destruction of the superficial portions of the dermis due to this exudation Small patches of proliferating epithelial cells could be found spreading through the exudate partially to cover the collagenous fibers Tissue sections showing the effect of tannic acid therapy revealed continued destruction of large portions of the dermis In addition, an extensive leucocytic exudate was seen at the base of the separating crust The process extended in some instances almost to the subcutis Small areas of epithelial regeneration could be seen in some sections

Specimens taken from 4 patients at 60 to 80 hours following the application of vaseline gauze and of tannic acid were available for study In those patients treated by vaseline gauze a layer of leucocytes and fibrin was seen on and in the superficial portions of the dermis Most of the leucocytes were neutrophils, but a few lymphocytes and monocytes could be seen Unquestionably there were some damage and destruction of the dermal collagenous fibers due to the infection present, but it was superficial in character In the sections which were obtained 70 hours following therapy, definite epithelial masses could be found spreading over the corium, in some

instances the epithelial cells appeared to be penetrating the leucocytic exudate.

Examination of sections treated with tannic acid showed the wounds to present a layered effect. The superficial portion was stained a deep blackish-brown because of a heavy precipitate of the tanning material. Collagenous fibers immediately beneath the superficial layer appeared as a glistening homogeneous mass staining lightly with eosin. The deepest layers were made up of strands of collagenous fibers taking an intense eosin stain. A few of these were smooth and homogeneous, and the entire layer was extensively infiltrated with leucocytes. This deep layer was thicker than the entire layer of damaged tissues in the vaseline treated wounds and contained an equal leucocytic exudate. In some sections all layers of the damaged dermis had separated from the underlying viable collagenous fibers while in others the superficial and middle layers were breaking away. These observations indicate that destruction of tissue is deeper than the firm eschar found covering the wound. Arm-like epithelial masses were spreading beneath the deep leucocyte invaded layer. Immediately beneath the newly formed epithelium focal collections of neutrophils and lymphocytes were found, and the surrounding dermal fibers stained normally with eosin. No granules of tannic acid were present.

Biopsy specimens from 2 patients were taken between 80 and 150 hours following application of vaseline gauze or tannic acid. During this period the leucocytic exudate in the vaseline gauze treated wounds was less marked than in the previous sections, and almost complete epithelization was seen. Beneath the newly formed epithelial cells a small amount of exudate was present. It consisted of focal collections of lymphocytes and plasma cells. Small masses of neutrophils could also be seen upon the epithelium. Sections from the wounds treated by tannic acid showed changes like those in the biopsies taken about 80 hours after therapy. Epithelization was almost complete. The leucocytic exudate beneath the epithelium had subsided and the superficial dermal fibers were lightly stained.

Biopsy specimens from 2 patients were obtained 5 to 10 days following the creation of

the wounds. In those treated by vaseline gauze epithelization was complete. Collagenous fibers beneath the epithelium stained less intensely than did the more mature deeper bundles, and a few lymphocytes were found among these light staining fibers. Sections taken from the tannic acid treated areas showed thick leucocytic exudates over the newly formed epithelial bridges. Beneath the epithelium focal collections of lymphocytes were present. At 5 days epithelial regeneration was complete but the epithelium was still quite thin.

#### SUMMARY

Many surgeons have suspected that tannic acid may have a destructive effect on tissues therefore they have advocated the use of non-irritating medicants for the treatment of burns. A review of the literature reveals little anatomic evidence to confirm or disprove the forementioned concept. A few experimental studies suggest that tannic acid probably injures normal tissues, but the evidence is not conclusive. We had an opportunity to compare the reaction of normal tissues to tannic acid and to vaseline impregnated gauze by applying them to donor sites of individuals who were receiving skin grafts.

Patients complained that the stiff eschar on donor sites treated with tannic acid caused considerable pain while comparable donor sites treated with vaseline gauze were relatively painless. On inspection it was found that the donor sites treated by vaseline gauze healed more quickly than those treated by tannic acid. Biopsy specimens of the treated donor sites were taken whenever the patients would submit to the procedure. A sufficient number of specimens were obtained to permit a study of tissue reactions to the medicant during a period ranging from several hours to 10 days. From study of these specimens we found that to form the eschar the tannic acid agents destroyed the dermis to a great depth. In addition, a marked leucocytic exudate was found beneath the eschar with further destruction of the collagenous bundles of the dermis. The portions of the epithelial structures contained in these layers were destroyed so that epithelization finally took place beneath the exudate. Vaseline gauze proved to

be nonirritating to the exposed dermis, hence only a mild red blood corpuscle and leucocytic exudate was found. The only visible damage to the dermis was in those cases showing some infection. Re-epithelization from the uninjured dermal glands was more prompt in the donor sites treated by tanning agents.

#### CONCLUSIONS

1 Donor sites heal more quickly with less discomfort when treated by vaseline gauze than when treated by tannic acid.

2 Tanning agents produce extensive tissue damage to the dermis to form the eschar while vaseline gauze produces a minimal damage.

#### REFERENCES

- 1 ANAGNOSTIDIS, NIKOS Deut Zschr Chir, 1939, 252 248-256
- 2 BETTMAN, ADALBERT G Northwest M, 1935, 34 46-51
- 3 DAVIDSON, EDWARD C Surg Gyn Obst, 1925, 41 202-221
- 4 LOEHR, W VON, and ZACHER, K Zbl Chir, 1939, 66 5-24
- 5 TAYLOR, FREDERIC J Am M Ass, 1936, 106 1144-1146

# STRUMA LYMPHOMATOSA

## Hashimoto's Disease

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THROUGHOUT the literature on diseases of the thyroid there exists a controversy as to the relationship of the entity first described by Riedel (29) called "*Essenhardt Struma*" to that first described by Hashimoto called "*Struma Lymphomatosa*." On the basis of a study of the literature and our own cases we have concluded that there is no relationship between the 2 diseases and will attempt to bring out data to support this contention.

### HISTORICAL REVIEW

Riedel (29, 30) in his original papers reported 5 cases of which 3 were males and 2 females. The striking clinical manifestation in all of the cases was the hardness of the tumor which suggested a malignant lesion. At operation this finding was confirmed and the thyroid was found to be attached to the trachea, the carotid artery and the internal jugular vein. Upon microscopic examination Riedel stated that he observed both spindle and round cells but when his drawings are inspected one is impressed by the dense infiltration of connective tissue. Lymphoid cells are present in only small numbers and lymph follicles are absent.

Hashimoto reported 4 cases, all of which were females. The tumors were firm but not hard. At operation there was fixation to the trachea but not to other tissues. Although there was rich infiltration with connective tissue the change he emphasized repeatedly was the presence of lymphocytes, diffuse and in the form of lymphoid follicles of varying size with germinal centers.

Ewing studied 4 cases and stated that in two of them very extensive and peculiar sclerosals had overtaken and largely replaced the lymphoid tissue. He concluded that "Hashi-

moto and Riedel have described the early and late stages of the same pathological process. Fibrosis and hyaline transformation become early and eventually as in Riedel's disease the enlarged gland becomes firm and dense.

Foot in a personal communication to Poir took the opposite view. He stated that "Hashimoto's struma has no connection with Riedel's struma and they represent two distinct processes—the one an overgrowth of lymphoid tissue followed later by fibrous invasion that may be more a metabolic than an inflammatory process—the other a fibrous overgrowth in response to some inflammatory stimulus. In Hashimoto's disease we have the lymphoid tissue growing as lymph follicles among the parenchymatous portion of the gland and crowding it out in that way but without the enormous fibrous reaction of Riedel's struma. In the latter the fibrous overgrowth seems to strangle the parenchyma slowly but certainly until it undergoes almost total atrophy and is replaced by dense wood masses of connective tissue. The lymphatic invasion in that case consists more of lymphocytes than of lymphoid tissue with germinal centers as is seen in Hashimoto's disease.

Joll (13) pointed out the confusion that exists in the literature in the interpretation of these two lesions. He described 51 cases of his own and 30 communicated to him. He emphasized in Riedel's struma the absence of diffuse lymphocytic infiltration and of lymphocytes, although admitting the presence of an occasional lymph follicle. He considered Hashimoto's disease a separate entity both clinically and pathologically from Riedel's struma.

Graham (6) thought that Riedel's struma was not always preceded by Hashimoto's disease and that Hashimoto's disease did not necessarily progress to Riedel's, and thought it improbable that there was any essential rela-

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tionship between the two. He stated that both clinical and microscopic findings were necessary to differentiate them and suggested that clinicians record the following data on their cases: age, sex, previous goiter, duration of symptoms, duration of goiter, extent and character of involvement of the thyroid, limitation of the process to the thyroid or extension beyond it (including more than a mere statement that the gland was adherent), adhesions to trachea as opposed to adhesions to surrounding structures, presence in the thyroid of adenomas, cysts, areas of calcification, frank inflammation, including small or large abscesses, presence or absence of hyperthyroidism or hypothyroidism before and after operation, amount of tissue removed, character of thyroid remaining and gross and microscopic findings.

Lee considered struma lymphomatosa and Riedel's struma separate entities. In his review of the literature in 1935 he accepted 26 cases as Hashimoto's and 90 as Riedel's disease. Only 1 case of struma lymphomatosa occurred in a male.

The only experimental work directly related to struma lymphomatosa which was found was done by McCarrison. He fed to rats a diet of American white flour, 72 to 80 parts, meat residue, 5 to 15 parts, olive oil, 8 parts, salt mixture containing 0.45 per cent potassium iodide, 5 parts, and distilled water, *ad lib*. Various modifications of this with greater or less amounts of white flour or with certain proportions of white flour replaced by starch were also used. Twenty-five per cent of the young rats fed on such diets had goiters of various sizes at autopsy. The goiters were found as early as 75 days and as late as 165 days after beginning the experiment and occurred more frequently in the female. Grossly the glands were glistening, fleshy, bright red or dark red, and 2.5 times normal size. The isthmus was usually prominent, thickened, and hardened. In the majority of instances the enlargement was bilateral with one lobe larger than the other but occasionally the enlargement was unilateral. His photomicrographs showed interacinar infiltration with lymphocytes with a follicle without a germinal center. He suggested that the occurrence of the disease in humans might be due to ingestion

exclusively of white flour or other vitamin-poor carbohydrates, vitamin-poor protein, vitamin-poor fats, and a scarcity of fresh fruits and green vegetables.

Boyden, Collier, and Bugher stated that "when one is afforded the opportunity to study pathological specimens from a series of cases, it is immediately apparent that different degrees of lymphocytic infiltration and lymph follicle formation as well as varying grades of fibrosis occur, not only in different glands but also in various portions of the same specimen. With this in mind, it becomes impossible to segregate them (Hashimoto's and Riedel's disease) into two distinct pathological entities." In discussing McCarrison's work they said "McCarrison considered this to be the result of dietary deficiency but it is equally good evidence of the possible rôle of iodine in the production of this type of thyroid disease."

Lee and McGrath (17), indirectly quoting Joll (14) and Graham and McCullagh (7) stated

"1. Hashimoto's struma is confined almost entirely to women over the age of 45 years while Riedel's disease usually occurs in adults but may appear at any age, and men are affected nearly as often as women."

"2. Regardless of operative treatment, patients with lymphadenoid goiter tend to develop myxedema, frequently preoperatively. Riedel's disease, even after extensive resection, rarely leads to defective function."

"3. Lymphadenoid goiter is diffuse from the outset and no part of the gland escapes. Localization to a lobe or part of a lobe is common in Riedel's struma."

"4. Widespread formation of delicate connective tissue is characteristic of the late stages of lymphadenoid goiter, while dense fibrosis comparable to scar tissue or keloid formation is found even in the earlier stages of Riedel's disease."

#### COLLECTED CASES

In a review of the literature it is difficult, from evidence reported, to select the true instances of Hashimoto's disease. This difficulty is due partly to the absence of an arbitrary standard, the diagnosis being a matter of opinion of the individual author, and partly to insufficient data in the report. In a complete review of the literature we found only 71 cases which were reported in sufficient detail to accept as unquestionable Hashimoto's disease. A few of the cases reported were not included because of incomplete data. Some cases which we considered true instances of struma lymphomatosa were originally reported



under another diagnosis most commonly that of Riedel's struma.

**Incidence.** Lee (18) at Presbyterian Hospital in New York found 3 cases in 1,800 thyroidectomies. Joll (13) 51 cases in 5,650 thyroidectomies while G. Keves in a personal communication to Joll recorded 25 cases in 1,600 patients in whom the thyroid had been removed. At the New York Hospital over a period of 10 years from 1932 to 1942 in 1,999 thyroidectomies there were 15 cases of Hashimoto's disease. Thus in 11,049 operations on the thyroid the incidence was one in 116 or slightly less than 1 per cent.

A summary of the data on the 71 cases of Hashimoto's disease is presented as follows:

The age in these cases varied between 14 and 75 years the average being 47 years. The majority of patients 39 presented themselves for treatment at 41 to 60 years of age. There were 2 patients in the 2d decade of life, 7 in the 3d, 12 in the 4th, 19 in the 5th, 20 in the 6th, 7 in the 7th, 4 in the 8th. There were 68 females and 3 males (10/16).

**Clinical manifestations.** In most of these patients a goiter or swelling in the neck was the chief complaint. The duration of symptoms was from 5 days to 32 years most commonly however from 1 month to 5 years. Loss of weight was more common than the gain which one might expect. Of those in which it was recorded 1 patients lost, 4 remained constant and 3 gained weight. The presence or absence of nervousness was mentioned in 21 patients of whom 13 complained that they were nervous while 8 said they were not nervous. The lesion grew slowly in 28 cases rapidly in only 3 and in 1 the rate of growth was slow until the 3 months before admission to the hospital and then rapid. Pressure symptoms noted were hoarseness, dysphagia, aphonia, tight feeling in the throat, pressure in the neck, stridor or substernal pressure, pulling sensation in the neck, coughing and change in voice. In 48 cases one of the above pressure symptoms was present while in only 3 it was noted that they were all absent. Other symptoms listed were loss of sleep, anorexia, palpitation, pain in neck, hypertension, fatigue, ability, menorrhagia, metrorrhagia, vertigo, headache, weakness, increased appetite, indi-

gestion, nausea and vomiting, swelling of ankles and hands, tachycardia, mental depression, fainting, tremor and hot flashes.

As regards the state of nutrition of these patients it is recorded that 22 were well developed and well nourished and 4 obese while in 1 patient malnutrition was noted. The blood pressures were given in 33 patients in 4. It was over 200 in 10, between 150 and 200, while in 16 it was 100 to 150. Only 1 instance of a blood pressure below 100 was found.

General statements in regard to the size of the gland indicate that the enlargement was slight in 16, moderate in 31 and marked in 24 cases. In the 71 collected cases 46 were described as showing uniform enlargement involving both lobes and the isthmus. In 6 only 1 lobe and the isthmus were affected. In 3 a single lobe was enlarged. In 16 the feature was not mentioned. The presence or absence of fixation was not mentioned in 43 cases in 16 it was stated that the thyroid was not fixed. Of the remaining cases 12 were described as fixed, in 3 the attachment being to the trachea, in 3 to other tissues including muscle or large vessels and in 6 the point of fixation was not given. Fixation is not a common feature.

The preoperative basal metabolic rate ranged from plus 63 to minus 23, tending on the whole to be slightly elevated. The average of the 41 recorded cases was plus 5. Postoperative tests on 20 patients at intervals ranged from 2 months to 8 years after operation. It was found to vary from plus 31 to minus 45 and the average minus 4. The average fall after operation was 19 points in the recorded cases.

**Operative findings.** The operative findings in regard to the presence or absence of uniformity of enlargement coincided with the clinical findings. Forty-four cases showed bilateral involvement with uniform changes. In 6 the isthmus alone, one lobe or one lobe and the isthmus were enlarged. No data were given on the others. The presence or absence of adherence is mentioned in 39 cases. Absence of adhesions was noted in 17, 23 were described as being attached to the trachea of which 10 were also adherent to muscles, large vessels and surrounding tissues. Vascularization was mentioned in 17 instances, being described as slight in 13 and marked in 4.

**Pathology Gross** The weight of the gland varied from 17 to 340 grams, the average being 91 grams. The gland was described as firm in 27 cases, hard in 20, and soft in 2.

**Microscopic** The thyroid acini tended to be small and atrophic with only a few showing areas of hyperplasia. In 38 cases the acini were atrophic, in 7 hyperplastic, in 4 normal, and in 4 atrophic with areas of hyperplasia. The acinar cells were usually small and low cuboidal with central nucleoli and were only rarely columnar. Colloid, in the main, was scant and in 24 cases was described as rare or little, in only 6 as normal, and in 7 it was noted that no colloid was present. Lymphoid elements were present in all cases, no case having been included unless it was stated that lymphoid elements were present or unless they could be seen in the photomicrograph. In 66 cases there was diffuse lymphoid infiltration and in 64 lymphoid follicles were present, in only 2 was a statement made that lymph follicles were not present. Germinal centers were described in only 7 cases although in none of the others was the statement made that such centers were absent. On the whole this lymphoid tissue was widespread and abundant. In 47 cases the amount of connective tissue was noted, in 17 of these it was scant or slight, in 20 moderate, and in 10 marked.

**Follow-up** Follow-up reports in the cases cited in the literature are unsatisfactory. Few late results were given and the metabolic rate, when noted at all after operation, was usually recorded only up to 6 months after thyroidectomy. Only 3 patients had basal metabolic tests as late as 2 years after operation.

#### NEW YORK HOSPITAL CASES

Table I gives a summary of the 15 cases of struma lymphomatosa treated at the New York Hospital.

**Clinical manifestations** The youngest patient in this group was 26 years of age, the oldest 60, and the average age 43.6 years. All patients in this group were women. In 13 patients the chief complaint was goiter, in 1 nervousness, and in 1 dyspnea and fatigability. The duration of symptoms varied from 9 months to 25 years, the average being 5 years. Weakness or fatigue was noted in 5 patients,

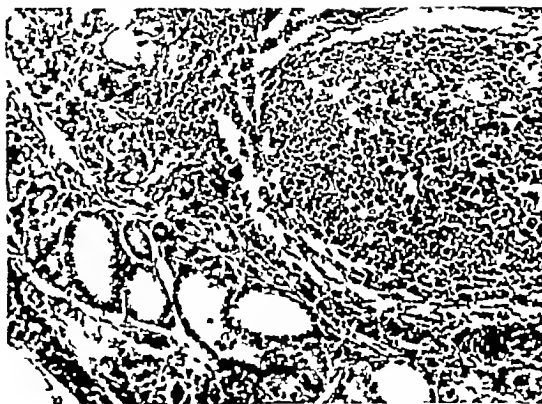


Fig 1 Photomicrograph showing thyroid acini with cuboidal epithelium containing small amounts of thin, poorly stained vacuolated colloid. A lymphoid follicle with a well formed germinal center is present and connective tissue is scant.  $\times 215$

weight loss in 3, and weight gain in 1, nervousness in 8, fever in none, slow growth of the goiter in 14, pressure symptoms such as hoarseness, dysphagia, or choking were noted in 6 patients and dyspnea on exertion in 7.

**Physical examination** Objectively fever was not found to be present in any patient. The pulse rate varied from 68 to 115 and averaged 93.6 per minute. The lowest blood pressure was 96/50 and the highest 204/100, the remainder of the readings being within normal limits. Seven patients were described as well developed and nourished, 1 as slightly obese, 4 as obese, and 1 as malnourished, while in 2 the state of nutrition was not stated. The gland usually was described as slightly to moderately enlarged, only 1 was said to be tremendously enlarged. All were referred to as nodular save 1 in which the presence of nodularity was not mentioned. In no case was fixation noted. Roentgenograms of the chest and neck taken before operation showed nothing abnormal except a soft tissue mass in the neck of 7 patients, a mass extending slightly into the thorax in 1 and tracheal deviation and compression in 1 case.

**Laboratory findings** The lowest blood count was 4,300, the highest 12,300. In 10 cases a differential count is recorded, the lymphocytes ranged between 23 and 47 per cent with an average of 36 per cent. There was no variation from normal of the other blood cells.

under another diagnosis, most commonly that of Riedel's struma.

**Incidence** Lee (18) at Presbyterian Hospital in New York, found 3 cases in 1,800 thyroidectomies. Joll (13) 51 cases in 5,650 thyroidectomies while G. Keynes in a personal communication to Joll recorded 25 cases in 1,600 patients in whom the thyroid had been removed. At the New York Hospital over a period of 10 years from 1932 to 1942 in 1,999 thyroidectomies there were 15 cases of Hashimoto's disease. Thus in 11,049 operations on the thyroid the incidence was one in 116 or slightly less than 1 per cent.

A summary of the data on the 71 cases of Hashimoto's disease is presented as follows:

The age in these cases varied between 14 and 75 years the average being 47 years. The majority of patients 39, presented themselves for treatment at 41 to 60 years of age. There were 2 patients in the 2d decade of life 7 in the 3d 12 in the 4th, 19 in the 5th 20 in the 6th 7 in the 7th 4 in the 8th. There were 68 females and 3 males (10/16).

**Clinical manifestations** In most of these patients a goiter or swelling in the neck was the chief complaint. The duration of symptoms was from 5 days to 32 years, most commonly however from 1 month to 5 years. Loss of weight was more common than the gain which one might expect. Of those in which it was recorded 11 patients lost 4 remained constant and 3 gained weight. The presence or absence of nervousness was mentioned in 31 patients of whom 13 complained that they were nervous while 8 said they were not nervous. The lesion grew slowly in 28 cases, rapidly in only 3 and in 1 the rate of growth was slow until the 3 months before admission to the hospital and then rapid. Pressure symptoms noted were hoarseness, dysphagia, aphonia, tight feeling in the throat, pressure in the neck, stridor or substernal pressure, pulling sensation in the neck, coughing and change in voice. In 48 cases one of the above pressure symptoms was present while in only 2 it is noted that they were all absent. Other symptoms listed were loss of sleep, anorexia, palpitation, pain in neck, hypertension, fatigue, inability, menorrhagia, metrorrhagia, vertigo, headache, weakness, increased appetite, indi-

gestion, nausea and vomiting, swelling of ankles and hands, tachycardia, mental depression, fainting, tremor and hot flashes.

As regards the state of nutrition of these patients it is recorded that 22 were well developed and well nourished and 4 obese. In 1 patient malnutrition was noted. The blood pressures were given in 33 patients in 6 it was over 200 in 10 between 150 and 200, while in 16 it was 100 to 150. Only 1 instance of a blood pressure below 100 was found.

General statements in regard to the size of the gland indicate that the enlargement was slight in 16 moderate in 31 and marked in 9 cases. In the 71 collected cases 46 are described as showing uniform enlargement, involving both lobes and the isthmus in 6 only 1 lobe and the isthmus were affected while in 31 single lobe was enlarged. In 16 this feature is not mentioned. The presence or absence of fixation was not mentioned in 43 cases in 14 it was stated that the thyroid was not fixed. Of the remaining cases 12 were described as fixed in 3 the attachment being to the trachea, in 3 to other tissues including muscle or large vessels and in 6 the point of fixation is not given. Fixation is not a common feature.

The preoperative basal metabolic rate ranged from plus 63 to minus 23, tending as the whole to be slightly elevated. The average of the 41 recorded cases was plus 5. Postoperative tests on 20 patients at intervals ranged from 2 months to 8 years after operation were found to vary from plus 3 to minus 45 and to average minus 4. The average fall after operation was 19 points in the recorded cases.

**Operative findings** The operative findings in regard to the presence or absence of uniformity of enlargement coincided with the clinical findings. Forty-four cases showed bilateral involvement with uniform changes in 6 the isthmus alone, one lobe or one lobe and the isthmus were enlarged. No data were given on the others. The presence or absence of adherence is mentioned in 39 cases. Absence of adhesions was noted in 17 13 were described as being attached to the trachea of which 10 were also adherent to muscles, large vessels, and surrounding tissues. Vasculature was mentioned in 17 instances, being described as slight in 3 and marked in 4.

*Pathology* Gross The weight of the gland varied from 17 to 340 grams, the average being 91 grams. The gland was described as firm in 27 cases, hard in 20, and soft in 2.

*Microscopic* The thyroid acini tended to be small and atrophic with only a few showing areas of hyperplasia. In 38 cases the acini were atrophic, in 7 hyperplastic, in 4 normal, and in 4 atrophic with areas of hyperplasia. The acinar cells were usually small and low cuboidal with central nucleoli and were only rarely columnar. Colloid, in the main, was scant and in 24 cases was described as rare or little, in only 6 as normal, and in 7 it was noted that no colloid was present. Lymphoid elements were present in all cases, no case having been included unless it was stated that lymphoid elements were present or unless they could be seen in the photomicrograph. In 66 cases there was diffuse lymphoid infiltration and in 64 lymphoid follicles were present, in only 2 was a statement made that lymph follicles were not present. Germinal centers were described in only 7 cases although in none of the others was the statement made that such centers were absent. On the whole this lymphoid tissue was widespread and abundant. In 47 cases the amount of connective tissue was noted, in 17 of these it was scant or slight, in 20 moderate, and in 10 marked.

*Follow-up* Follow-up reports in the cases cited in the literature are unsatisfactory. Few late results were given and the metabolic rate, when noted at all after operation, was usually recorded only up to 6 months after thyroidectomy. Only 3 patients had basal metabolic tests as late as 2 years after operation.

#### NEW YORK HOSPITAL CASES

Table I gives a summary of the 15 cases of struma lymphomatosa treated at the New York Hospital.

*Clinical manifestations* The youngest patient in this group was 26 years of age, the oldest 60, and the average age 43.6 years. All patients in this group were women. In 13 patients the chief complaint was goiter, in 1 nervousness, and in 1 dyspnea and fatigability. The duration of symptoms varied from 9 months to 25 years, the average being 5 years. Weakness or fatigue was noted in 5 patients,

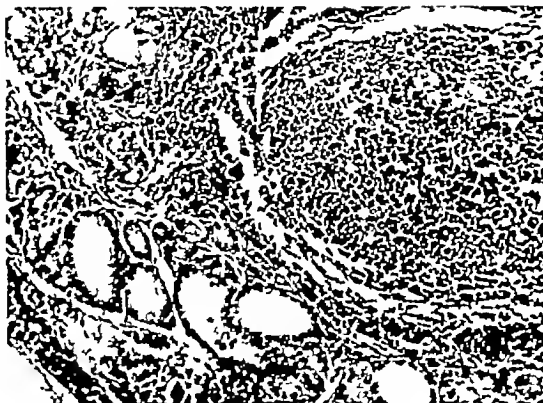


Fig 1 Photomicrograph showing thyroid acini with cuboidal epithelium containing small amounts of thin, poorly stained vacuolated colloid. A lymphoid follicle with a well formed germinal center is present and connective tissue is scant.  $\times 215$

weight loss in 3, and weight gain in 1, nervousness in 8, fever in none, slow growth of the goiter in 14, pressure symptoms such as hoarseness, dysphagia, or choking were noted in 6 patients and dyspnea on exertion in 7.

*Physical examination* Objectively fever was not found to be present in any patient. The pulse rate varied from 68 to 115 and averaged 93.6 per minute. The lowest blood pressure was 96/50 and the highest 204/100, the remainder of the readings being within normal limits. Seven patients were described as well developed and nourished, 1 as slightly obese, 4 as obese, and 1 as malnourished, while in 2 the state of nutrition was not stated. The gland usually was described as slightly to moderately enlarged, only 1 was said to be tremendously enlarged. All were referred to as nodular save 1 in which the presence of nodularity was not mentioned. In no case was fixation noted. Roentgenograms of the chest and neck taken before operation showed nothing abnormal except a soft tissue mass in the neck of 7 patients, a mass extending slightly into the thorax in 1 and tracheal deviation and compression in 1 case.

*Laboratory findings* The lowest blood count was 4,300, the highest 12,300. In 10 cases a differential count is recorded, the lymphocytes ranged between 23 and 47 per cent with an average of 36 per cent. There was no variation from normal of the other blood cells.

TABLE I—NEW YORK HOSPITAL CASES

Case Number	Primary Diagnosis	Incision Used	Child Karyotype	Patho- logy	Type of Incision	Ovarian Pathology			Maxillary Pathology			Follow up
						Size Cm.	Uniformity	Granulosa	Acute	Lymphoid infiltration	Metast.	
100	Uterine cancer				20	40	Not uniform	Cystic degeneration	Medium infiltration	Diffuse, complete infiltration	Small	11 years No metast.
101	Uterine cancer				20	40	Uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
102	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
103	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
104	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
105	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
106	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
107	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
108	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
109	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
110	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
111	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
112	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
113	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
114	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
115	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
116	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
117	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
118	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
119	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.
120	Uterine cancer				20	40	Not uniform	Normal	Atrophic	Diffuse, complete infiltration	Small	11 years No metast.

NOTE: The above cases were all of the type in which the tumor was found to be of the type of the above.

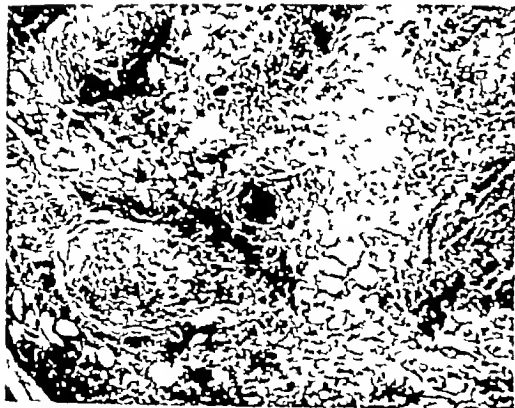


Fig 2. Photomicrograph showing numerous small thyroid acini with scant colloid and several lymphoid follicles of varying size, some with germinal centers.  $\times 105$



Fig 3. Photomicrograph showing a few small thyroid acini with diffuse infiltration with lymphocytes and fine connective tissue stroma.  $\times 105$

The Wassermann reaction was negative in the 10 cases in which it was recorded. The basal metabolic rate before operation was below normal in 7 cases, above normal in 3, normal in 1 case, and not recorded in 4 cases. Following operation and before the patient was discharged from the hospital the basal metabolic rate was minus in 4 cases, plus in 1, and not recorded in 8 patients.

**Diagnosis.** The preoperative diagnosis was nontoxic nodular goiter in 9 cases, adenoma in 2, cystadenoma in 1, Graves' disease in 2, and toxic nodular goiter in 1 case.

**Operative findings.** At operation, uniform enlargement was noted in 10 cases, in 3 cases of bilateral enlargement one lobe was more enlarged than the other, in 1 case the isthmus was mainly affected and in 1 the isthmus and a single lobe were enlarged. In only 1 case was the gland adherent to the trachea and in only one gland was marked vascularity noted. In 14 cases a subtotal thyroidectomy was carried out, in the remaining case the isthmus and one lobe were removed.

**Pathology.** Gross. The smallest specimen removed weighed 7 grams, the largest 177 grams, the average weight was 66 grams. As regards consistency, 5 were described as firm, 4 as soft, and 2 as hard. In 8 cases the goiter was described as uniform, while 6 were designated as nodular. The color varied from pearly white through light yellow, yellow, pinkish gray to dark red or brown. In 7 cases

colloid was present, while in 1 it was absent, in 7 cases the presence or absence of colloid was not noted.

**Microscopic.** Uniform changes were noted in 11 of the 15 cases while in the other 4 changes were not uniform. Lymphoid elements were diffuse in 13 cases, in the other 2 there were scattered follicles and slight interacinar infiltration. In the cases with diffuse infiltration there were numerous follicles in all save 1 which showed quite dense interacinar infiltration. The follicles varied in size from  $1/3$  to  $1/30$  of a low power field and were considered small in 8 cases, small to moderate in 6, and large in 1 case. For the most part they were round or oval in shape. Germinal centers were present in some or all of the follicles in 14 cases, while in only 1 were there no germinal centers.

Thyroid acini varied from small ( $1/30$  low power field) to fairly large ( $1/2$  low power field). In 1 case acini resembled those seen in fetal adenoma. In all cases the thyroid acini were round to oval and in 7 some of the acinar cells were in the form of syncytial masses. The acinar cells were flattened in 3 cases, low cuboidal in 2, and fairly high cuboidal in 10. Cytoplasm in all was dull and granular. The nucleus was central or basal and round in all sections, usually with one or more nucleoli. In all glands colloid was present. Many acini contained cellular debris which resembled degenerated acinar cells. The amount of

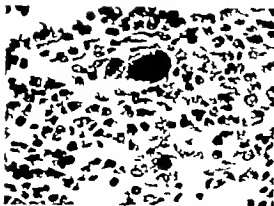


FIG. 4. Photomicrograph showing pseudogiant cell back is actually disintegrating thyroid acini. There is infiltration of lymphocytes and plasma cells. The supporting connective tissue stroma is scant in amount and fine in texture.  $\times 40$ .

colloid was small in 8 fairly large in 3 and in the other 4 was described as small to fairly large. The color by Masson trichrome stain was orange throughout, and vacuolation of the colloid was present in all instances varying in degree from slight to marked.

Connective tissue was scant in 9 moderate in 3 and fairly dense in 3. The texture was fine in 12 and fairly coarse in 3 but even when the texture was fine the trabeculae were dense. Blood vessels were present in the trabeculae in normal numbers in 12 fairly numerous in 2 and numerous in 1 case. In all instances the vessels were small save 1 in which they were designated as small to medium. No true giant cells were seen in any of the sections. In 6 cases no plasma cells were seen in 6 they were present in small numbers and in 3 numerous. They were found outside the follicles and in the interacinar tissue. Polymorphonuclear neutrophils were seen only in the blood vessels.

**Follow-up.** We have follow up records on 13 of the 15 cases and all were examined by both authors. Eight of the 15 patients have been followed for more than 2 years 5 for more than 3 years 3 for more than 5 years and 1 for 6½ years since operation. All patients except 1 showed clinical evidence of hypothyroidism after operation and had lowered basal metabolic rates the 1 patient had a basal rate of plus 16 and showed mild hyperthyroidism. The basal metabolic rates varied with the

amount of thyroid extract administered and was given after operation to 10 patients. In no case was there a recurrence of goiter. Anemia became marked in 3 patients following operation and in both it was difficult to control. Six patients gained weight, lost 7 and 4 who were taking thyroid extract.

#### EVALUATION

The typical case of struma lymphomatosa may be described as follows. A female 40 to 45 years of age presents a goiter of long standing which has grown slowly. She complains of weakness, fatigability, slight nervousness and some pressure symptoms. Examination reveals moderate obesity. The thyroid gland is moderately enlarged fairly uniform in consistency and nodular. The basal metabolic rate usually is slightly below normal. The only other laboratory finding of diagnostic value is a slight relative lymphocytosis.

At operation the gland shows fairly uniform enlargement of both lobes and the isthmus. It may be slightly attached to the trachea but usually not to other structures and its vascularity is normal or slightly decreased.

The gross pathological examination reveals a firm white to yellow or brown nodular thyroid weighing from 60 to 90 grams and with little colloid. Microscopic examination shows the thyroid acini to be atrophic with cell granular cuboidal epithelium. The presence of lymphoid elements is the most striking feature and is in the form of diffuse interstitial infiltration with numerous lymph follicles with germinal centers. Trabeculation usually is fairly marked but otherwise the connective tissue is rather fine and in normal amount.

This study sheds no light on the cause of this lesion. A history of previous iodine administration was observed in too few of our cases and mentioned too rarely in the cases reviewed to be of etiological significance. A past history of toxicity which might indicate that the lymphoid process resulted from a "burned out" toxic thyroid likewise was rare. Dietary deficiency suggested as a possible cause of the disease by McCarrison, perhaps warrants further study. With our advance knowledge of vitamins since his paper was published some experiments along this line

might be of interest Struma lymphomatosa certainly seems to be a physiologic or metabolic rather than a neoplastic or inflammatory disease

All of our patients were subjected to thyroidectomy as were all of the cases collected from the literature except 2, so there is little direct evidence of the course the disease would take if not interrupted by removal of the gland It is possible only to speculate as to whether without operation the symptoms would progress and more and more of the thyroid acini be destroyed by the increase in lymphoid elements It is evident from this study that the disease can be controlled by, and does not recur after, subtotal thyroidectomy, that the pressure symptoms and nervousness are relieved after such an operation and that the signs of myxedema can be counteracted by the administration of adequate amounts of thyroid extract to keep the basal metabolic rate within normal limits Renton, Charteris and Heggie proposed the use of radiotherapy in the treatment of struma lymphomatosa and reported a case of a woman with complaints of goiter and pressure symptoms in which the diagnosis was established by biopsy of the central portion of the isthmus and which was treated with a "radium collar" Their report included a photomicrograph which showed unquestionable struma lymphomatosa Thirteen days after irradiation was started the goiter had completely disappeared and they reported the patient as "perfectly well" 5 years later In view of the radiosensitivity of lymphoid tissue and the relative radioresistance of thyroid acini, this procedure may prove to be beneficial in true, microscopically proved cases of struma lymphomatosa Radiotherapy presumably would not cause the hypothyroidism which follows thyroidectomy and hence would obviate the need of thyroid extract

#### CONCLUSIONS

Hashimoto's disease is considered an entity entirely separate and distinct from Riedel's struma both clinically and pathologically Subtotal thyroidectomy for struma lympho-

matosa relieves the symptoms and may be said to cure the disease but the majority of patients after operation develop hypothyroidism of sufficient severity to require the administration of thyroid extract Two fields for further study have been suggested the importance of vitamin deficiency as a causative factor and irradiation as a form of treatment

#### REFERENCES

- 1 BOYDEN, A M, COLLIER, FRED G, and BUGHER, J C *West J Surg*, 1935, 43 547
- 2 CLUTE, HOWARD, ECKERSON, L B, and WARREN, SHIELDS *Arch Surg*, 1935, 31 419
- 3 EMERSON, CLARENCE *Nebraska M J*, 1935, 20 58
- 4 EWING, JAMES *Benign Granuloma of Thyroid*, Riedel's Struma Neoplastic Diseases 3d ed, p 961 Philadelphia W B Saunders, 1928
- 5 FERNANDEZ, FERNANDO L *Tr 3rd Internat Goiter Conf and Am Ass Goiter*, 1938, pp 234-236
- 6 GRAHAM, ALLEN *West J Surg*, 1931, 39 681
- 7 GRAHAM, A, and MCCULLAGH, E P *Arch Surg*, 1931, 22 548
- 8 HASHIMOTO, H *Arch klin Chir*, 1912, 97 219
- 9 HELLWIG, C ALEXANDER *Arch Path*, 1938, 25 838
- 10 HEYD C G *Surg Clin N America*, 1929, 9 493
- 11 HOWARD, LAURENCE *Am J Surg*, 1934, 23 565
- 12 JAFFE, R H *J Am M Ass*, 1937, 108 105
- 13 JOLL, CECIL A *Brit J Surg*, 1939-1940, 27 351
- 14 Idem *Diseases of the Thyroid Gland* London Heinemann, 1932
- 15 JOYCE, T M, MENNE, F B, and ZELLER, W E *Arch Surg*, 1941, 42 338
- 16 KEARNS, J E, JR. *Ann Surg*, 1940, 112 421
- 17 LEE, C MARSHALL, JR, and McGRATH, E J *Surgery*, 1937, 2 238
- 18 LEE, J GORDON *Arch. Surg*, 1935, 31 982
- 19 LEHMAN, JAMES A. *Tr 3rd Internat Goiter Conf and Am Ass Goiter*, 1938, pp 237-244
- 20 LESTER, CHARLES W *Am J Cancer*, 1934, 21 103
- 21 MALLORY, TRACY B *N England J M*, 1935, 213 1140
- 22 MCCARRISON, R. *Brit M J*, 1929, 1 5
- 23 MCCLINTOCK, JOHN C, and WRIGHT, ARTHUR W *Ann Surg*, 1937, 106 11
- 24 MCQUILLAN, ARTHUR S *Tr 3rd Internat. Goiter Conf and Am Ass Goiter*, 1938, pp 212-219
- 25 MEANS, JAMES H *The Thyroid and its Diseases* Page 502 Philadelphia Lippincott, 1937
- 26 POER, DAVID H, DAVISON, T C, and BISHOP, E L *Am J Surg*, 1936, 32 172
- 27 POLOWE, DAVID *Arch Surg*, 1934, 29 768
- 28 RENTON, J M, CHARTERIS, A A, and HEGGIE, JAMES F *Brit. J Surg*, 1938-1939, 26 54
- 29 RIEDEL, B M C L *Deut. Gesellsch Chir*, 1896, 25 101
- 30 Idem *Münch med Wschr*, 1910, 57 1946
- 31 SHAW, A F B, and SMITH, R P *Brit. J Surg*, 1925-1926, 13 93
- 32 SMITH, L W, and CLUTE, H. *Am J M Sc*, 1926, 172 403
- 33 WINGATE, H F *Brit J Surg*, 1929-1930, 17 264



# MELANOEPIITHELIOMA (MELANOSARCOMA MELANO-CARCINOMA MALIGNANT MELANOMA) OF THE EXTREMITIES

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FOR the purpose of evaluating the methods of treatment and prognosis we have reviewed the clinical and pathological material available in a series of 155 cases in which a diagnosis of melanoeplithelioma of the extremity was made at the Mayo Clinic during the 24 years from 1916 to 1939 inclusive. We realize that a lesion of this type is relatively rare and the prognosis has long been recognized as a grave one. In 107 of the 155 cases we found sufficient data on which to base conclusions, and in this group we reviewed the histopathological material and corroborated the original diagnosis. Forty-eight cases of the series were excluded from our study. In 33 of these 48 cases the patients had arrived at the clinic in hopeless condition; multiple metastatic lesions were present and operation or microscopic verification of the diagnosis was not indicated; in 11 cases the original pathological diagnosis was not substantiated on re-examination of the tissue; and in 4 cases was not available for confirmation of the original diagnosis.

The purpose of limiting our study to those cases in which the tumor is located in an extremity was so that we may evaluate the relative value of amputation and local excision in the treatment of such lesions. Broders and MacCarty, in 1916, and Farrell, in 1923, reported a series of cases in which lesions of this type were located in all parts of the body and in which the patients were seen at the Mayo Clinic.

## HISTORY

In 1806, Dupuytren first described melanoma although some descriptions of this condition in bones appeared in the literature in the latter part of the 18th century. Paget and Virchow recognized that malignant changes took place in moles, and the latter divided these changes into sarcomatous and carcinomatous degeneration. The fact that the cellular picture was so varied stimulated many investigators in their study for the true origin of these tumors. There is still

divergence of opinion concerning their origin; some authorities think that they are of epithelial origin. The leaders of this school are Linn and Dawson. The latter has written an excellent monograph on the subject. The belief that melanomas of mesodermal origin arises from the fact that many of them appear to be of sarcomatous structure (1/8). Still other investigators think they arise from the end organs of the peripheral sensory nerves and are neuroectodermal in origin (6/9).

Since melanoeplithelioma is a difficult condition to cure, many forms of treatment have been employed. This same statement of course holds true of the treatment of all malignant disease. After a trial of ointments, caustery and embolus, all treatment may be abandoned and the condition considered incurable. Wide excision and block dissection, including the regional glands and amputation of the diseased extremity have been undertaken without encouraging results. Roentgen and radium treatment frequently have been tried alone or in combination. All the procedures mentioned, but even this type of treatment has not proved to be a solution of the problem.

## INCIDENCE OF AGE AND SEX

The age and sex distribution in this series of 127 patients has been summarized in Table I. The youngest patient was 12 years of age and the oldest 76 years. The average age was 47.6 years. It is of interest to note that 50.5 per cent of the patients were between 40 and 60 years of age, and the remainder were distributed above and below these ages. The percentage of females affected was 58.9 per cent or 17.8 per cent higher than that of the males which was 41.1 per cent. This is not what we would expect to find if trauma were considered one of the etiological factors. In 31.5 per cent of the cases, however, there was a definite history of some type of trauma or irritation at the site of the initial lesion. Most frequently it resulted from a shoe rubbing or a nail puncture of the foot. In the remainder or 66.5 per cent, trauma was not mentioned in the case history.

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## LOCATION AND TYPE OF LESION

The location of the primary lesion in this series of cases is given in Table II. It is obvious that melanoepithelioma has a predilection for the lower extremity, since in this group of patients 76.7 per cent of the primary lesions were located on the legs and the other 23.3 per cent on the arms, 30.9 per cent of the total number, however, were located on the foot exclusive of the toes. The subungual type of lesion comprised only 9.3 per cent of this series and the greater percentage, 6.5 per cent, of these were located beneath the fingernails. The lesions were distributed nearly equally on the right and left sides of the body.

The type of the primary lesion was described variously by the patients, 40 of whom stated that the original lesion was a "mole", 25 noted the appearance of a tumor first, 20 described a "black, brown, or purple spot", 12 first noted an "ulcer or abrasion", 7 a "blood blister", and 3 stated that the tumor arose from a "callus". At the time of their first visit at the clinic 58, or 54.2 per cent, had an ulcerating lesion at the site of the primary lesion. This in some instances was the result of failure in healing after excision of the primary lesion and in others the result of degeneration in the original tumor. At the time of the original visit, 41 patients had discernible metastatic lesions in addition to the primary lesion which was present.

TABLE I—AGE AND SEX OF PATIENTS IN VERIFIED CASES OF MELANOEPITHELIOMA OF THE EXTREMITIES, 1916-1939 INCLUSIVE<sup>1</sup>

Age, years	Total		Males		Females	
	Num ber	Per cent	Num ber	Per cent	Num ber	Per cent
10-19	2	1.9	—	—	2	3.2
20-29	13	12.1	4	9.1	9	14.3
30-39	16	15.0	5	11.4	11	17.5
40-49	25	23.4	11	25.0	14	22.2
50-59	20	27.1	13	29.5	16	25.3
60-69	15	14.0	7	15.9	8	12.7
70+	7	6.5	4	9.1	3	4.8
Total	107	100	44	100	63	100
Youngest	12 years		21 years		12 years	
Oldest	76 years		76 years		74 years	
Average	47.6 years		50.5 years		45.6 years	
Sex, per cent	100		41.1		58.9	

<sup>1</sup>Pathological sections and tissue have been re-examined and the previous diagnosis confirmed.

TABLE II—LOCATION OF PRIMARY LESION IN CASES OF MELANOEPITHELIOMA, 1916-1939 INCLUSIVE

Location	Total		Right		Left	
	Num ber	Per cent	Num ber	Per cent	Num ber	Per cent
The subungual	3	2.8	2	66.7	1	33.3
Toe other part	15	14.0	9	60.0	6	40.0
Foot (except toes)	33	30.9	11	33.3	22	66.7
Leg	10	17.8	11	57.9	8	42.1
Thigh	12	11.2	8	66.7	4	33.3
Finger subungual	7	6.5	5	71.4	2	28.6
Finger other part	3	2.8	—	—	3	100.0
Hand (except fingers)	2	1.9	—	—	2	100.0
Forearm	6	5.6	4	66.7	2	33.3
Arm	7	6.5	1	14.3	6	85.7
Total	107	100	51	47.7	56	52.3

Metastasis of this lesion apparently occurs through all possible routes. In many of the cases the surrounding tissues were invaded by direct extension, in some cases local stellate extension occurred about the original lesion via the skin lymphatics. Direct metastasis through the deep lymph vessels to the regional lymph nodes and beyond occurred in many cases and in others invasion of the blood vessels was apparent, for the cells had been carried throughout the body by the blood stream which had produced widespread metastasis including the central nervous system and the skin. Metastatic lesions as well as the primary lesion may or may not be pigmented, but in all cases the cellular structure proved the true nature of the lesion.

## SYMPTOMS

Enlargement of the primary lesion was the most frequent type of onset noted. Forty-one of the 107 patients complained of some associated pain. As the tumor enlarged, the surface became friable and was prone to bleed when irritated and, as we have stated previously, ulceration occurred in a fair percentage of the cases. In another type the first sign may be an increase in the deposit of pigment without much enlargement of the lesion. Later stellate pigmented growths may appear about the primary lesion. In still another variety the first sign may be metastatic enlargement of the regional lymph nodes and an innocent appearing mole which has undergone malignant changes may be found distally on the extremity. No pre-existing lesion is necessary and the first symptoms

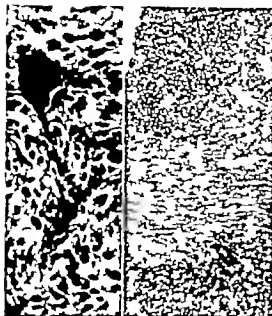


FIG. 1. a, left, Non-melanotic melanocarcinoma. Itb great variation in the size and shape of the cells and frequent mitotic figures.  $\times 300$ . The patient died 3 year following excision of tumor from the heel. b, Areas of pigmentation and non-pigmented bearing cells within the same tumor. Strand and acinar formation is evident in the lower left portion. High gives rise to so-called melanocarcinoma type of tumor.  $\times 35$ .



FIG. 2. Metastatic involvement of lymph nodes of large round and oval type cells, both pigmented and non-pigmented.  $\times 75$ . The patient died 3 year following the removal of tumor and regional nodes.

which are observed in a great number of cases may be the appearance of an entirely new pigmented region or of a tumor which shows progressive enlargement.

#### DIAGNOSIS

Any new lesion or pre-existing one of the skin which enlarges or ulcerates should be viewed with suspicion. This is especially true of a lesion about the nail bed. If it is pigmented, a presumptive diagnosis is easily made. However in the non-pigmented type of melanocarcinoma the true nature of the lesion is not evident until macroscopic examination of the tissue has been made.

*Differential diagnosis.* The final diagnosis of melanocarcinoma rests with the pathologist following his study of the histological picture. However several clinical entities may be confused with it they are benign pigmented moles, blue nevus, lentigo, verruca senilis, pigmented basal cell epithelioma, melanotic carcinoma of the breast and hemorrhage any one of which may simulate melanocarcinoma.

#### HISTOLOGICAL PICTURE

Little can be added to the knowledge of the histological picture of these tumors that has not already been brought out by Dawson in his excellent monograph. The cells themselves are pleomorphic and vary from round ones to spindle-shaped ones as shown in Figure 1a. Branched and polyhedral cells may be present and each always their size varies greatly. The nuclei are large vesicular stain only lightly and frequently contain mitotic figures. The cells contain a variable amount of pigment the basal cells contain the most. These basals may be filled completely or even appear to be bursting with it, and the pigment also may be seen deep within the subcutaneous tissue. In tumors of the non-melanotic type pigment is not seen though the cellular structure was characteristic in every other respect. Within the same tumor may be seen regions of deep pigmentation or regions completely devoid of pigment as demonstrated in Figure 1b. The cellular arrangement may take one of several forms. They may be arranged in sheets of cells with little intercellular substance



Fig 3 Spindle cell or sarcomatous type of melanoma with only light pigmentation  $\times 222$  The patient is living without evidence of metastasis 2 years following amputation of an arm



Fig 4 Strand and acinar like arrangement of cells or so-called melanocarcinoma  $\times 94$  The patient is living without evidence of metastasis 8 years following amputation of a toe

and no definite pattern, the predominant cells may be round as shown in Figure 2, or spindle-shaped as shown in Figure 3. In other tumors the cells form in strands and have an acinus-like arrangement which gives rise to the adenocarcinomatous appearance of some of these tumors, as shown in Figures 1, b and 4. Perivascular and perilymphatic masses of cells are evident in some tumors and not infrequently malignant cells are included within the lumen of blood vessels and lymphatic spaces. Within the same tumor the cellular structure and arrangement may differ and vary from a carcinomatous nature to the spindle cell sarcomatous type of tumor, usually, however, only one type of cellular picture is predominant. As a rule metastatic lesions are of the same cellular structure and pattern as the primary tumor, but they may or may not be pigmented. In the early stages it may be difficult to distinguish the tumor from a benign pigmented cutaneous lesion, but the true invasive nature of the cells of melanoma may be determined by a careful study of the tissue, as demonstrated in Figures 5 and 6.

#### TREATMENT

In 50 of the 107 cases some form of treatment had been given elsewhere. Some of the more common methods mentioned by the patients cannot be included as proper means of treatment, namely, heat and massage, ointment, pastes, caustics, inadequate cautery and electrodesiccation, and curettage of ulcers. The types of treatment which have been employed at the clinic and those used elsewhere are listed in Table III. In far the greatest number of cases either a wide excision of the local lesion including even metastatic lesions in nodes or amputation of the affected digit or extremity was employed. In a few of the cases amputation was done as a palliative measure because of the distressing nature of the primary growth.

#### RESULTS AND PROGNOSIS

To analyze and obtain survival rates in a study of a condition, such as melanoma, in which the nature of the lesion, the time of institution of treatment, and the types of treatment are so varied, is a difficult task. On the extremities where the lesion is so open to inspection and the

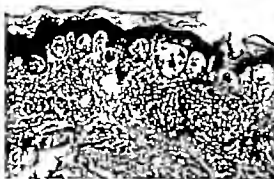


FIG. 5. Tissue from lesion which had been excised from the foot of patient who is living without evidence of metastasis 6 years following operation.  $\times 47$ . Examination with high power magnification demonstrated infiltration of malignant cells into presarcomatous tissue.

onset of symptoms points to the actual onset of malignant changes, the basing of the survival rate on the time the tumor actually began should be considered. The proof of malignancy, however, waits biopsy. In this study the 3 and 5 year survival rates have been computed from the onset of symptoms and also from the time that treatment was instituted.

In a series as small as this one, if the cases were divided in accordance with all the detailed types of treatment employed, the number in each group would be too small—none on which to base any conclusions. For that reason we have divided our cases into only three groups: (1) those in which surgical treatment had not been given; (2) those

TABLE III.—TREATMENT OF MELANOPHTHLEIOMA, 1906-1939 INCLUSIVE.

Treatment at clinic	Total	Previous treatment elsewhere	
		Excision	Amputation
No treatment			
Local only*			
Irradiation only*		10	
Excision of lesion†	20		
Excision of lesion and metastatic nodes	22	19	
Amputation	23		
Total	97	29	0

\*Local phosphorus was administered in 3 cases. In cases in which this was the only form of treatment, in case the only other treatment was excision, this case looked under the heading, irradiation only. In all the cases excision of the primary lesion was performed, as 2, excision of the primary lesion and metastatic nodes and in 1, amputation.

†Which or without irradiation, amputation was performed in 1 case of excision of the primary lesion, in all cases of excision of the primary lesion and metastatic nodes, and in 1 case of amputation.

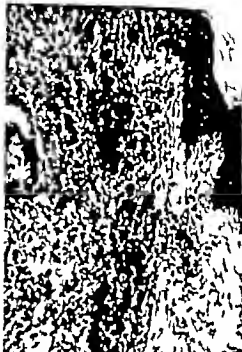


FIG. 6. Transition from benign to malignant epithelium and deep penetration of malignant cells into subcutaneous tissue.  $\times 14$ . The patient is living one year after excision.

in which amputation had been performed and (3) those in which local excision of the primary lesion and of local recurrences, as performed with or without excision of the regional nodes.

The computed survival rates are given in Tables IV and V. It is interesting to note that in all the highest percentage of survivals occurred following excision. Cases 1 and 2 in this paper are examples of such survival. Many of the amputations are performed in cases in which the lesion was more extensive while excision was carried out incidentally at times, then a operation for a unassociated lesion, as being done. This accounts to some extent for the better results obtained in the group in which excision was performed but after all factors have been taken into consideration it is felt that when it is possible wide excision of the lesion and of all suspicious nodes offers the patient as is possible a better result does amputation. In those cases in which a deep involved local excision is not feasible and amputation is the procedure of choice.

In only 1 case (Case 3) in this series of 97 the melanophtthelioma respond to irradiation in the

opinion of the radiologists. In a condition with as grave a prognosis as that which we have in melanoepithelioma, every patient certainly is entitled to even the questionable benefits that may be derived from irradiation with or without associated operation.

In this type of malignant neoplasm, as in no other, the unknown equation of individual resistance to a tumor of high grade of malignancy appears to play a part. Several patients (Case 4 for example) survived a long period after repeated excision of the local and regional recurrences.

#### REPORT OF ILLUSTRATIVE CASES

**CASE 1** A woman, aged 24 years, was seen at the Mayo Clinic on August 22, 1922, at which time she stated that since birth she had had a somewhat elevated papillomatous lesion on the lateral aspect of the left thigh and that it had been increasing in size during the past 10 years with more rapid growth during the last 2 years. Examination revealed a tumor, about 3 centimeters in diameter, which had become a soft pedunculated papillomatous mass. Excision was performed on August 25, 1922, and pathological examination of the tissue removed revealed a typical melanoepithelioma. Because it was felt that this lesion was in its early stages and excision had been complete, no further treatment was advised. In reply to an inquiry letter, which was dated August 19, 1940, the patient stated that she was well, did not have any sign of recurrence of the tumor, and had been well during the past 18 years.

**CASE 2** A woman, aged 57 years, was examined at the Mayo Clinic on February 4, 1921. She stated that she had had a blood blister on the palmar surface of the web of the thumb of the left hand and that, in 1919, she had removed this hard, black lesion with a plaster, but it had recurred in September of that year. The lesion then had been removed by means of an electric needle and 6 roentgen treatments had been given. Furthermore, the following year the tumor had recurred and she had sought further treatment.

Because of the suspicious nature of the lesion biopsy was performed at the clinic and the pathological examination



Fig 7 Case 3 Large round and oval cells with little intercellular substance and no pigment  $\times 850$

verified the clinical diagnosis of melanoepithelioma. On February 10, 1921, a wide excision of the tumor was performed after which a course of radium treatment was given. In reply to an inquiry received on August 21, 1940, the patient stated that she was living and without known metastasis, 19 years following treatment at the clinic.

TABLE IV—THREE AND 5 YEAR SURVIVAL RATES FROM TIME THAT TREATMENT OF MELANOEPITHELIOMA OF THE EXTREMITIES WAS INSTITUTED

Group	Total*	Traced	Lived 3 or more years following treatment		Total*	Traced	Lived 5 or more years following treatment	
			Num ber	Per cent of traced cases			Num ber	Per cent of traced cases
No surgical treatment	6	6	0		6	6	0	
Amputation	23	22	8	36.4	20	19	4	21.1
Excision	67	63	25	39.7	60	57	17	29.8
Total	96	91	33	36.3	86	82	21	25.6

\*Inquiry as of January 1, 1941. The 3 year group comprises the patients treated 3 or more years prior to the time of inquiry that is 1937 or earlier; the 5 year group comprises those treated in 1935 or earlier.

TABLE V—THREE AND 5 YEAR SURVIVAL RATES FROM TIME OF ONSET OF SYMPTOMS OF MELANOEPITHELIOMA OF THE EXTREMITIES

Group	Total*	Traced	Lived 3 or more years after onset		Total*	Traced	Lived 5 or more years after onset	
			Num ber	Per cent of traced cases			Num ber	Per cent of traced cases
No surgical treatment	7	7	3	42.9	7	7	2	28.6
Amputation	26	23	15	65.2	25	23	9	39.1
Excision	68	65	45	69.2	65	62	28	45.2
Total	101	95	63	66.3	97	92	39	42.4

\*Inquiry as of January 1, 1941. The 3 year group comprises the patients who had onset of symptoms 3 or more years prior to the time of inquiry that is 1937 or earlier; the 5 year group comprises those who had onset of symptoms in 1935 or earlier.

**CASE 3.** A woman, aged 33 years, as seen at the Mayo Clinic on February 20, 1920, at which time she stated that she had noticed a tumor of the right calf and swelling of the right groin for months prior to admission and that these had been enlarging gradually. The tumor was removed from the calf and the pathological examination revealed melanocapthelioma (Fig. 7). On February 26, 1920, the enlarged and normal lymph nodes were dissected from Scarpa's triangle on the right, and metastatic involvement was found. Subsequently the lesion in the calf which was removed on March 3, 1920, recurred and still later that in the right inguinal region which was removed on August 9, 1920. After this last recurrence the patient received inter-feronin and radium treatment to the leg and groin. The patient returned to the clinic in 1936, at which time she had no complaint except for tenderness of the region to which irradiation had been directed. At this time the radiologist made note to the effect that the tumor apparently was radionecrotic. In reply to an inquiry received on August 2, 1942, the patient stated that she had been in good health and did not have any evidence of recurrence 20 years after the institution of treatment.

In this case the prognosis apparently was hopeless at the time treatment was instituted, but in spite of this the patient survived and enjoyed 20 years of life. The fact that recurrence of the lesion took place following each excision but did not do so following irradiation would lead us to believe that the latter had been the arresting procedure.

**CASE 4.** A woman, aged 47 years, as first seen at the Mayo Clinic on April 9, 1911, at which time she stated that she had noticed a nodule on the calf of her left leg for the past 3 years, that about 3 years previously it had enlarged and was removed by her physician, but during the recent months a lump had recurred at the site of excision.

Wide excision of the tumor of the calf was performed and on the same day pathological examination of the tissue revealed melanocapthelioma (Fig. 8). Healing occurred promptly and the patient was not seen again until May 4, 1916, at which time she returned to the clinic because of recurrence at the site of operation. Removal was carried out again and the pathological examination revealed the same condition. Three months later the patient again reported to the clinic with evidence of enlarged right inguinal glands; these were removed and the pathological examination again revealed melanocapthelioma. At this time an intensive course of radium and roentgen treatment was given to the groin. The patient died on May 27, 1917, 5 years following her first admission to the clinic.

In this case we have an illustration of the length of life possible after metastases has occurred. Although the treatment given did not cure the patient, it did increase the length of her life.

#### CONCLUSIONS

We have reviewed those cases of melanocapthelioma of the extremities which were encountered at the Mayo Clinic during a 24 year period.

It is apparent that if treatment had not been instituted the patients would have died, whereas

20.8 per cent of the patients who were treated by excision survived 5 years or more from the time treatment was instituted. This group included many cases in which the lesions were small at the time the patients were seen during the early stages of the disease.

In those cases in which the lesion was more extensive and of long duration amputation was the most common type of treatment, and in this group there was a 5 year survival rate of 21 per cent from the time treatment was instituted.

None of the patients in that group in which irradiation was the only form of treatment survived 3 years from the time treatment was instituted at the clinic. Irradiation was employed in conjunction with operation in numerous cases. In those cases in which the patient refused amputation and in those in which the lesion was inoperable. This form of treatment should not be condemned as further advancement in the science of radiology and its clinical application may prove it of more benefit than is now apparent.

Melanocapthelioma may be present for long periods of time before the seriousness of the nature is determined or recognized, and the condition may be activated by medullary treatment. Therefore in the authors opinion the treatment of choice for melanocapthelioma is wide excision with removal of regional lymph nodes or amputation. In cases in which tumors do not appear to be increasing in size or showing evidence of ulceration, wide local excision would appear adequate.

#### REFERENCES

1. BUCKNER, S. W. Arch. Derm. Syph. 57:6 Col. 818-833.
2. BRONNER, V. C. and McCARTY, W. C. Surg. Gyn. Obst. 9: 6, 1, 7-12.
3. D. 1874, J. W. Edinburgh M. J. 35, 32, 38-40.
4. DUFFLEMAN. Quoted by Pennington. (After observations on the History Pathology and Treatment of Cancerous Diseases. Vol. 3 London J. Clin. 358).
5. FARRELL, H. J. Arch. Derm. Syph. Ch. 70, 39, 6-14.
6. FOOT, V. C. Am. J. Path. 132, 8, 12, 137.
7. PALFREY, J. Lectures on Surgical Pathology 77, 637-644, 3d ed. Philadelphia Lindsay & Blak.
8. RUSSELL, H. CO. Ueber das Melanocapthelioma. Ber. path. Anat. 807, 477-499.
9. SOLDAN, M. and M. WERRE. Quoted by F. and J. von Brit. M. J. 1905, 2: 852-855.
10. URETA, P. G. The Histopathology of the Diseases of the Skin. P. 745. New York The Macmillan Co. 1905.
11. VINCOW, R. Arch. 72, 75, 146.

# SCHWANNOMAS (NEURILEMOMAS) IN THE HEAD AND NECK

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THE present study is based on an analysis of 10 cases of schwannoma arising in the tissues about the head and neck, these were observed at the Memorial Hospital from 1936 through 1942. Such neoplasms are known to occur in almost every part of the body, but when situated in the head and neck they present special diagnostic and therapeutic problems which seem to us to warrant a separate discussion.

**Definition.** A specific form of encapsulated and essentially benign tumor of the sheath of peripheral nerves was first described in 1908 by Verocay (35, 36) who introduced the term "neurinoma." Mallory proposed the name "perineurial fibroblastoma" for this tumor to designate an origin from the fibroblast. The term "schwannoma" (from the sheath of Schwann) has been widely used, apparently because the bulk of available evidence favors the schwannian theory of histogenesis. Since there is a difference of opinion as to whether this tumor is of schwann cell (ectodermal) or fibroblastic (mesenchymal) origin, and since it is generally agreed that this is a tumor of the neurilemma, then Stout's contribution—"neurilemoma"—appears reasonably specific. Before Stout's publication, Ewing had suggested the name "neurilemmoma" for these tumors.<sup>1</sup>

## ETIOLOGY

**Incidence.** Schwannoma is a rare tumor. Its general incidence can be judged by the fact that it occurs only about 1/50th as frequently as cancer of the lip. The 10 cases (in the head and neck) herein reported comprise 43 per cent of all schwannomas (23 cases) encountered at the Memorial Hospital during the 6 year period—1936 through 1942. In most other reports on this tumor, the proportion arising in the head and neck is less than in our series. In Stout's series of 50 cases—the largest collection of schwannomas to appear in the literature—only 26 per cent were situated above the level of the clavicle. The higher pro-

portion in this location found at the Memorial Hospital may possibly be due to the relatively large number of patients with all varieties of head and neck tumors—about 1600 new cases yearly—admitted to our clinic.

In our series, the tumors were distributed as follows: neck, 7 cases; soft tissues of the nose, 1 case; retropharyngeal area, 1 case; retrotonsillar area, 1 case. The preponderance of origin in the neck, as compared to the head, has been noted by others and can be explained by the relatively large number of peripheral nerve trunks grouped in this area. Askanazy, Figi, and Stout have each reported single cases of schwannoma in the retropharyngeal, retrotonsillar, and nasopharyngeal areas, respectively. Other authors have reported instances of this tumor in such regions as the eye (8, 18), orbit (5, 6, 28, 29), eyelid (12), maxillary sinus (33), floor of mouth (4), tongue (3, 12, 16, 17, 33), hard palate (2, 22, 33), larynx (15, 30, 32, 33), and salivary glands (33).

Two of our tumors (Cases 1 and 7) had their origin from the phrenic nerve. Figi, Freifeld, and Stout have described schwannomas which arose from the cervical sympathetic nerves. Sekiguchi and Ojje and Cutler and Gross have each encountered a schwannoma with origin from the vagus nerve. The tendency of this tumor to originate in the 8th cranial nerve is well recognized by neurosurgeons.

**Age and sex.** In our series, the oldest patient was 68 years and the youngest 23 years old at the time of admission. These tumors, however, may appear at any age. Stout has described 4 cases in which the tumors apparently became evident during the first year of life. Both sexes were equally affected. In our series, there were 5 males and 5 females.

**Causative factors.** An analysis of our cases reveals no evidence of a common causative factor. Many observers have commented on the frequent association of schwannomas with the multiple neurofibromatosis of von Recklinghausen. That there was no instance of this recorded in our series is probably of little significance since the records give no evidence that the examiner particularly looked for neurofibromatosis. The association of pigmented naevi (Case 2), a ganglion (Case 9)

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<sup>1</sup>Other terms encountered in the literature were peripheral glioma, lemmoma, encapsulated neurofibroma, neurinoma, sarcomatodes, false neuroma, and fibroma molluscum.



CASE 3. A woman, aged 3 years, seen at the Mayo Clinic on February 20, 1920, at which time she stated that she had noticed a tumor of the right calf and swelling of the right groin for 6 months prior to admission and that these had been enlarging gradually. The tumor, as removed from the calf and the pathological examination revealed melanopithelioma (Fig. 7). On February 20, 1920, the enlarged and normal lymph nodes were dissected from Scarpa's triangle on the right, and metastatic involvement was found. Subsequently the lesion in the calf, which was removed on March 8, 1920, recurred and still later that is the right inguinal region, which was removed on August 9, 1920. After this last recurrence the patient received intensive roentgen and radium treatment to the leg and groin. The patient returned to the clinic in 1926 at which time she had no complaint except for tenderness of the regions in which irradiation had been directed. At this time the radiologist made note of the effect that the tumor apparently was radioresistant. In reply to an inquiry received on August 9, 1920, the patient stated that she had been in good health and did not have any evidence of recurrence 20 years after the institution of treatment.

In this case the prognosis apparently was hopeless at the time treatment was instituted, but in spite of this the patient survived and enjoyed 20 years of life. The fact that recurrence of the lesion took place following each excision but did not do so following irradiation would lead us to believe that the latter had been the arresting procedure.

CASE 4. A woman, aged 47 years, as first seen at the Mayo Clinic on April 9, 1915, at which time she stated that she had noticed a mole on the calf of her left leg for the past 5 years; that about 1 year previously it had enlarged and, as removed by her physician, but during the recent months a lump had recurred at the site of excision.

Wide excision of the tumor of the calf, as performed and on the same day pathological examination of the tumor revealed melanopithelioma (Fig. 8). Healing occurred promptly and the patient was not seen again until May 4, 1916, at which time she returned to the clinic because of recurrence at the site of operation. Removal, as carried out again and the pathological examination revealed the same condition. Three months later the patient again reported at the clinic with evidence of enlarged right inguinal glands; these were removed and the pathological examination again revealed melanopithelioma. At this time an intensive course of radium and roentgen treatment was given to the groin. The patient died on May 27, 1927, 12 years following her first admission to the clinic.

In this case, however, an illustration of the length of life possible after metastases has occurred. Although the treatment given did not cure the patient, it did increase the length of her life.

#### CONCLUSIONS

We have reviewed those cases of melanopithelioma of the extremities which were encountered at the Mayo Clinic during a 24 year period.

It is apparent that if treatment had not been instituted the patients would have died, whereas

29.8 per cent of the patients who were treated by excision survived 5 years or more from the time treatment was instituted. This group included many cases in which the lesions were small and the patients were seen during the early stages of the disease.

In those cases in which the lesion was more extensive and of long duration amputation was the most common type of treatment, yet in this group there was a 5 year survival rate of 1 per cent from the time treatment was instituted.

None of the patients in that group to which irradiation was the only form of treatment survived 3 years from the time treatment was instituted at the clinic. Irradiation, especially in conjunction with operation in numerous cases, in those cases in which the patient refused an operation and in those in which the lesion was inoperable. This form of treatment should not be condemned as further advancement in the science of radiology and its clinical application may prove it of more benefit than is now apparent.

Melanopitheliomas may be present for long periods of time before the seriousness of their nature is determined or recognized, and their condition may be activated by medicamentous treatment. Therefore, in the authors' opinion the treatment of choice for melanopithelioma is wide excision with removal of regional lymph nodes or amputation. In cases in which tumors do not appear to be increasing in size or showing evidence of ulceration, wide local excision could appear adequate.

#### REFERENCES

1. BICKEL, S. W. Arch. Derm. Syph. Ch., 1920, 8: 8-33.
2. BROOKS, V. C. and McCURRY, W. C. Surg. Gen. Obst. 9: 6, 1-3.
3. DIXON, J. W. Edinburgh M. J. 1912, 12: 309-14.
4. DEPUYRE, quoted by Pemberton, *Oper. (4th ed.)* sections on the History, Pathology and Treatment of Cancerous Diseases. (ed. 8 London) J. Churchill, 1919.
5. LARRELL, H. J. Arch. Derm. Syph. Ch., 1914, 29: 0-24.
6. FORT, V. C. Am. J. Path. 1914, 8: 311-17.
7. FOSTER, J. Lectures on Surgical Pathology, 1910, 630-645, 6th ed. Philadelphia: Lindsay & Blakely, 1905.
8. RUSSETT, H. GO. Ueber das Melanopitheliom. Ber. path. Anat. 1877, 477-499.
9. SODER and MANNING. Quoted by F. H. Jones, Brit. M. J. 1920, 1: 51-53.
10. URBAN, P. G. The Histopathology of the Diseases of the Skin. P. 745. New York: The Macmillan Co., 1906.
11. VINCOW, R. Virchow's Arch. 1920, 240: 1-10.

at the opposite end of the fibers. This produces a palisading pattern, which is so characteristic of schwannoma (Fig 2). The cells and fibers also form whorls.

Areas of fibrosis and necrosis are invariably encountered in this portion of the tumor. Hemorrhage, too, is a common occurrence, as well as thromboses within thick walled blood vessels. This necrotizing process produces areas in which fibers have disappeared and only cells remain, or areas in which the reticulum is devoid of cells.

In the type B tissue, there is no orderly arrangement of cells and fibers, and therefore no palisading of nuclei is seen. This phase is characterized by an accumulation of intracellular fluid and the appearance varies from one of edema (Fig 3), which dissects the tissue apart, to microcystic degeneration (Fig 4).

Specific staining techniques for the identification of axis cylinders were not carried out in any of our specimens.

Although the schwannoma has generally been considered a benign tumor, atypical areas containing hyperchromatic and pleomorphic cells and suggestive of early malignant changes were observed in Cases 4 and 8 (Fig 5).

**Histogenesis.** The histogenesis of these tumors has been a subject of controversy for many years. One group of investigators, led by Penfield, contends that the tumor is of fibroblastic origin, and therefore, a mesenchymal neoplasm. On the other hand, the hypothesis first proposed by Verocay (35, 36) and supported by Masson states that the tumor arises from the cells of Schwann and that it is, therefore, an ectodermal neoplasm.

Those who support the connective tissue theory argue that the tumor cells resemble fibroblasts



Fig 4 Further edema has produced microcystic degeneration. Palisades have been completely destroyed (Antoni type B tissue).

morphologically, and that only fibroblasts can produce collagen. Recently, however, Masson has produced experimental schwannomas and has been able to trace both the experimental and spontaneous tumors back to the schwannian syncytium. Masson, and Murray and Stout (24, 25) have demonstrated by means of tissue cultures that the cells of these specific nerve sheath tumors are morphologically and physiologically similar to the cells of Schwann. Also, Murray and Stout have cultivated the tumor *in vitro* and demonstrated the derivation of reticulin fibers from the cells of Schwann.

The bulk of available evidence, therefore, appears strongly to favor the schwannian theory of origin.

#### SYMPTOMS AND CLINICAL COURSE

The tumors are probably always of long duration when first discovered. In 5 of our cases,

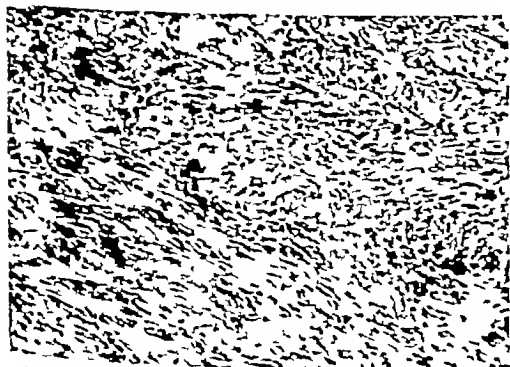


Fig 5 A schwannoma which was suspected of early malignant transformation because of atypical areas shown above. The cells are hyperchromatic and pleomorphic; there is no orientation between fibers and cells. This tumor was clinically and anatomically benign (Case 4).



Fig 6 Tissue which was obtained by aspiration biopsy of a retrotonsillar schwannoma. Palisading pattern is definite. The structure at the left end of the field is part of a blood clot to which the tumor tissue is seen to be attached (Case 10).



Fig. 1. Resection of cervical schwannoma showing the irregular mottled appearance and necrosis. Note cyst formation. This tumor was located at the carotid bifurcation and was of phrenic nerve origin (Case 7).

and a synovium (Case 3) appeared to be merely coincidental.

#### PATHOLOGY

**Gross pathology.** All the tumors in this collection were encapsulated. They varied from 1.5 centimeters to 7 centimeters in greatest diameter. The majority of the specimens were globular or fusiform and smooth, although in a few instances the surface was nodular and even distinctly lobulated. The consistency was soft and sometimes fluctuant; this characteristic may be explained by the cystic degeneration that these neoplasms usually undergo. Occasionally a growth was firm and fibrous.

The cut surface was glistening and revealed a multiplicity of patterns. Most often irregular mottled areas were seen ranging from pink to yellow to pearl gray in color. Occasionally these patches were arranged in whorls. The central

portion of the tumor was almost always necrotic. Hemorrhages were frequently scattered throughout, especially beneath the capsule (Fig. 1). Areas varying from cystic degeneration to spaces containing fluid were encountered, and in such specimens definite fluctuation was elicited before the tumor was cut.

The tumors of the neck presented distinctive and uniform anatomic features. They were sharply demarcated from the surrounding structures. With the exception of one tumor which was located in the supraclavicular area, the others were situated beneath the upper one third of the sternocleidomastoid muscle and usually anterior to the carotid vessels. Frequently a large nerve was seen to disappear into the tumor; most of the nerve fibers, however, could often be stripped away from the capsule. The smaller tumors confined themselves to this location, but the larger tumors extended beyond this area to the mandible, the pharyngeal wall, and even to the transverse processes of the adjacent cervical vertebrae.

The capsule was well supplied with blood vessels which did not penetrate into the substance of the tumor, while the vascularity of the tumor was generally poor.

**Histopathology.** For many years, it has been customary to divide the histologic picture of this nerve sheath tumor into the type A and type B tissues of Antoni. This classification is so specific and descriptive as to warrant its continued use.

Type A tissue is characterized by a reticulus of fine, long fibers which pass between the cells. The cells and their nuclei are elongated and cytoplasmic processes stream out to form a network. The intracellular fibers are in a parallel arrangement, while the elongated cell nuclei are lined up



Fig. 2. Characteristic microscopic appearance of schwannoma. The nuclei are lined up at the opposite end of the fibers, producing typical palisades (Antoni type A tissue).

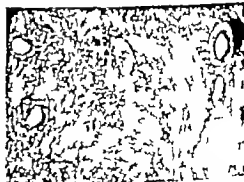


Fig. 3. Accumulation of intracellular fluid has caused the fibers apart, breaking up the palisades. Note the thick-walled blood vessel, one of which contains thrombi (Antoni type B tissue).

at the opposite end of the fibers. This produces a palisading pattern, which is so characteristic of schwannoma (Fig 2). The cells and fibers also form whorls.

Areas of fibrosis and necrosis are invariably encountered in this portion of the tumor. Hemorrhage, too, is a common occurrence, as well as thromboses within thick walled blood vessels. This necrotizing process produces areas in which fibers have disappeared and only cells remain, or areas in which the reticulum is devoid of cells.

In the type B tissue, there is no orderly arrangement of cells and fibers, and therefore no palisading of nuclei is seen. This phase is characterized by an accumulation of intracellular fluid and the appearance varies from one of edema (Fig 3), which dissects the tissue apart, to microcystic degeneration (Fig 4).

Specific staining techniques for the identification of axis cylinders were not carried out in any of our specimens.

Although the schwannoma has generally been considered a benign tumor, atypical areas containing hyperchromatic and pleomorphic cells and suggestive of early malignant changes were observed in Cases 4 and 8 (Fig 5).

**Histogenesis.** The histogenesis of these tumors has been a subject of controversy for many years. One group of investigators, led by Penfield, contends that the tumor is of fibroblastic origin, and therefore, a mesenchymal neoplasm. On the other hand, the hypothesis first proposed by Verocay (35, 36) and supported by Masson states that the tumor arises from the cells of Schwann and that it is, therefore, an ectodermal neoplasm.

Those who support the connective tissue theory argue that the tumor cells resemble fibroblasts

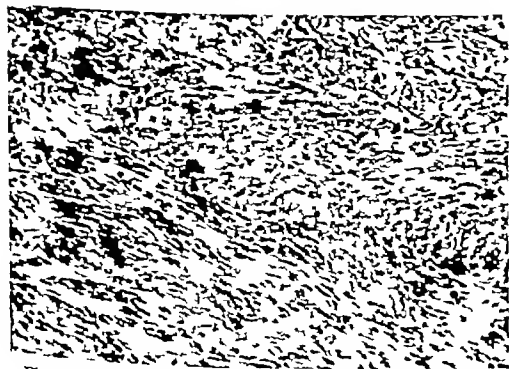


Fig 5. A schwannoma which was suspected of early malignant transformation because of atypical areas shown above. The cells are hyperchromatic and pleomorphic, there is no orientation between fibers and cells. This tumor was clinically and anatomically benign (Case 4).



Fig 4. Further edema has produced microcystic degeneration. Palisades have been completely destroyed (Antoni type B tissue).

morphologically, and that only fibroblasts can produce collagen. Recently, however, Masson has produced experimental schwannomas and has been able to trace both the experimental and spontaneous tumors back to the schwannian syncytium. Masson, and Murray and Stout (24, 25) have demonstrated by means of tissue cultures that the cells of these specific nerve sheath tumors are morphologically and physiologically similar to the cells of Schwann. Also, Murray and Stout have cultivated the tumor *in vitro* and demonstrated the derivation of reticulin fibers from the cells of Schwann.

The bulk of available evidence, therefore, appears strongly to favor the schwannian theory of origin.

#### SYMPTOMS AND CLINICAL COURSE

The tumors are probably always of long duration when first discovered. In 5 of our cases,



Fig 6. Tissue which was obtained by aspiration biopsy of a retrotonsillar schwannoma. Palisading pattern is definite. The structure at the left end of the field is part of a blood clot, to which the tumor tissue is seen to be attached (Case 10).

according to the patients' histories, the growth had been present for from 6 to 10 years, and in 1 case for 1 year. In the 4 remaining cases the patients stated that the tumors had been noted 5 months, 8 months, 5 months and 3 weeks respectively. In the latter group, since the growths were all 2.5 to 5 centimeters in greatest diameter the patients' statements must be considered unreliable and one must conclude that schwannomas are probably slowly growing and of long duration when first discovered.

The most common and often the only symptom is the physical presence of the tumor. In our series, over one half of the patients had no other complaint on admission. Since the tumor originates in nerve tissue one might logically expect pain to be frequent and characteristic, but in the present series this symptom was present in only 3 cases and in only 1 case was it severe. When present, pain appears to be due to pressure of the tumor on adjacent nerves, rather than to the nerve of origin. Another symptom which might be expected was mechanical obstruction to swallowing. This was encountered in our 2 pharyngeal cases (Cases 3 and 6).

A Horner's syndrome was encountered once in our series (Case 2) and persisted despite complete removal of the cervical tumor. This may be attributed to pressure by the tumor on the cervical sympathetic plexus with irreparable nerve damage. One may also speculate whether such a tumor may have had its origin from a cervical sympathetic nerve, even though the nerve could not be identified as part of the tumor. Schwannomas with origin from the cervical sympathetic nerves have been described by Figg, Freilich, and Stout. A temporary Horner's syndrome occurred as a postoperative complication following excision of a cervical tumor (Case 9). This phenomenon has been encountered by others and can be attributed to tissue changes or possibly to trauma following surgical manipulation.

On physical examination the tumors were always found to be single, circumscribed, soft, movable and not tender. In our cases, they possessed no characteristic features differentiating them from the average encapsulated clinically benign tumor.

The clinical course of schwannoma is apparently benign even without treatment. Since the diagnosis cannot be made except by histological examination it naturally follows that in all reported cases the tumors have been excised. There is no way of knowing what would happen if the growths are left untreated, except if the diagnosis is made by aspiration biopsy. So far, no aspirated

tumor has been observed for any long period without treatment. In our Case 10 the diagnosis was made by aspiration biopsy, but the patient has been followed only 1 year during which time there has been no apparent change in the size or symptoms. In Case 7 the tumor had been noted 10 years previously and yet it had reached a size of only 5 centimeters in diameter on admission and there was no complaint except the presence of the mass.

#### DIAGNOSIS

In our series, the diagnosis of schwannoma was not made clinically. In a single instance before a microscopic report was returned. In the average case of schwannoma of the neck, the long duration of the tumor, the absence of any growth in the mouth or pharynx which might point to a cervical metastasis, and the discrete soft character of the tumor mass should lead the experienced clinician to a tentative diagnosis of a benign primary tumor. Further than that, no one can proceed on the clinical aspects alone. The possible varieties of discrete benign soft part tumors which can occur in the head and neck are so numerous that little is to be gained by an attempt at a more exact clinical diagnosis than that a given tumor is encapsulated and probably benign.

*Differential diagnosis.* In our series, 7 of the tumors occurred in the neck, and in these the following tentative clinical diagnoses had been made before aspiration biopsy or operation, respectively: lipoma, submaxillary salivary gland tumor, cervical lymph node metastasis, hyphomatoma, neurogenic sarcoma, carotid body tumor and cystic hygroma.

As has previously been mentioned, an attempt at exact differential diagnosis by clinical means alone and without biopsy of discrete soft part tumors of the head and neck is largely an academic exercise and is, furthermore, dangerous to the welfare of the patient if taken too seriously. Good oncologic practice demands first that a clinically demonstrable field of growth be discovered and next that tissue be obtained from it most readily accessible and safest site. Until histological section has been examined under the microscope the diagnosis is only tentative.

Some authors (3, 27) have commented on the similarity between schwannomas in the region of the carotid bifurcation and carotid body tumors. Both forms of tumor are rare. Carotid body tumors can seldom be diagnosed clinically except by one characteristic feature, that is, pulsation of the carotid artery over the tumor itself. This pulsation is due to the deep origin of carotid body tumors in

the crotch of the carotid bifurcation and the tendency of these tumors to grow inward and to push the artery outward. Since schwannomas supposedly arise from the sheaths of the nerves, it has been thought that mobility in the horizontal plane and fixation in the vertical plane are important diagnostic signs and that for this reason, they might also be confused with carotid body tumors which are supposedly characterized by these same limitations in mobility. The practical importance of these diagnostic signs, in our opinion, have been somewhat overemphasized.

**Aspiration biopsy** This procedure was used as a means of preoperative diagnosis in 6 cases and a positive report was given by Dr. Fred Stewart, pathologist of the Memorial Hospital, in 5 cases. In the 1 instance in which a single aspiration biopsy gave a negative result, it is probable that further attempts would have revealed the histological character of the tumor, as was demonstrated in Case 5. The practical significance of aspiration biopsy in the diagnosis of cervical tumors cannot be overemphasized. The importance of knowing whether one is dealing with a benign growth like schwannoma, metastatic cancer, carotid body tumor, or a primary localized malignant tumor is obvious. It is only by aspiration biopsy that an accurate preoperative diagnosis can be made in clinically doubtful cases.

This procedure is of special value in the retropharyngeal and retrotonsillar tumors, in which operative intervention may be hazardous. A retrotonsillar schwannoma may simulate a primary tumor of the tonsil. One of our patients (Case 10) was subjected to x-radiation and tonsillectomy before aspiration biopsy finally revealed the character of the tumor (Fig. 6).

#### TREATMENT

In all the cases previously reported, the tumors have been excised and the diagnosis made first histologically on the surgical specimen. Even though it may be comforting to the surgeon and the patient that the procedure turned out to be the proper one and permanently successful, nevertheless, under such circumstances, the treatment in any given case was not actually selected for schwannoma but rather for a tumor of unknown or at least uncertain character. It is probable that the same surgeon had also excised other tumors which to him appeared identical, but which unfortunately proved to be metastatic cancer or some other growth best not treated by local excision. At the present time, the histological character of most accessible tumors can be determined by aspiration biopsy and the most

suitable form of treatment selected on the basis of that information.

When the certain diagnosis of schwannoma has been made, the management of the growth should be decided after a consideration of the known anatomy and clinical course of the tumor. If it produces a visible alteration in the surface contour, the growth should be locally excised (enucleated) for psychologic and cosmetic reasons.

If the patient has any undue fear or other objection to surgery, one is hardly justified in urging operation. Second, when the tumor is situated in a less accessible area, such as the pharynx, surgical removal in certain cases will be attended by definite risk, especially in older subjects. Such a situation is illustrated by our Case 10. In this patient the tumor bulged in the tonsillar region with a marked pulsation over its apex. The patient was in poor general condition and had marked hypertension. Under such circumstances even though the patient prefers an operation, the prudent surgeon is justified in deferring the procedure indefinitely with the confidence that in any case, progress of the growth is slow and malignant degeneration improbable.

Surgical excision was performed in all of our cases except 2—the retropharyngeal and retrotonsillar cases—in whom operation was considered to be unjustifiably hazardous for these benign tumors with minimal symptomatology. No technical difficulties were encountered in those operated on. In every case, the mass was encapsulated and enucleation was performed with ease, even in those instances in which the tumor was adherent to the carotid vessels or to the intervertebral lamina. The vascularity of this neoplasm was a characteristic of some practical significance. The capsule was well supplied with blood vessels which did not penetrate into the substance of the tumor. If the capsule was first incised, no bleeding was encountered on enucleation of the mass. When the capsule had been torn or when an attempt was made to enucleate the tumor without preliminary incision of the capsule, troublesome bleeding followed.

Supplementary roentgen therapy was given one patient (Case 8) because the tumor cells were hyperchromatic and pleomorphic (Fig. 5). Another patient received postoperative radium element pack therapy because of the possibility that tumor tissue may have been left high in the neck posterior to the carotid sheath (Case 2). As our familiarity with the behavior of schwannomas has increased, we now believe that in retrospect, these 2 cases should not have received radiation therapy. Two of our patients (Cases 3 and 10) were

TABLE 1.—TABULATION OF CASE REPORTS

Case No. (Initials) Age Sex	Date of ad- mission	Clinical features	Size of tumor (pre- and post-ther- apy) cm.	Super- ficial lesion	Treatment	Subsequent course	Remarks
D M M	1-9-36	Mass on neck of mouth		Not done	Radiation and possible therapy followed by surgical removal	No recurrence after year follow-up	Simulated, covered body lesion. Fibrous mass seen
A M	1-11-37	Mass on neck of mouth duration History trauma. Horner's syndrome		Not done	Excision, followed by roentgen clinical pack therapy	No recurrence after year follow-up. Presence of Horner's syndrome	Simulated, covered body lesion. A simulated tumor involving posterior of face
E G F	4-1-36	Pain on swallowing of neck duration Retropharyngeal mass		Positive	Observation	No enlargement after year follow-up. No reappearance of tumor	Radiation possible therapy before admission. No and lesion upon entry of abdominal wall.
J M M	10	Swelling over base of mouth duration		Not done	Excision	No recurrence. Died year follow-up tumor (perforation involving larynx operated)	Masses over mouth as in suggested use of early and late changes
M L F	1-11-36	Mass on neck of mouth duration		Positive (after third layers, low)	Excision	No recurrence after year follow-up	Simulated, covered body lesion
H M by M	1-26-37	Mass on neck of neck duration. Pain over lesion of mouth duration		Positive	Excision	No recurrence after year follow-up	Simulated, covered body lesion. Early and late changes
M J M	11-30	Mass on neck of 10 years duration		Negative	Excision	No recurrence after year follow-up	Simulated, covered body lesion. Early and late changes
L L F	4-1-37	Mass on neck of mouth duration		Not done	Excision, followed by roentgen therapy	No recurrence after month follow-up	Possible origin from base of pharynx. Microscopic exam showed squamous cell metastatic changes
E G E	11-32	Mass on neck of mouth duration. Pain on head and neck of mouth duration		Positive	Excision	No recurrence after month follow-up Masses over mouth	Simulated, covered body lesion. Temporary post-operative Horner's syndrome. In- volvement of larynx and trachea
D R F	1-10-37	Pain on swallowing of neck duration Retropharyngeal mass		Positive	Observation	No enlargement after year follow-up	Excision therapy and local therapy before admission tumor was not noted by operation biopsy

\*Reported by courtesy of Dr. George T. Pack.

[Reported by courtesy of Dr. Lloyd C. Green.

subjected to roentgen therapy before coming to the Memorial Hospital and in Case the patient received preoperative radium and roentgen therapy but tumor regression was not observed in any of these patients.

Like all tumors of nerve tissue origin, schwannomas are apparently highly radioresistant and therefore radiation should never be employed. Small doses have no possibility of influencing the growth. Large doses are particularly objectionable because even though ineffective on the tumor they cause grave sequelae in adjacent normal tissues.

#### PROGNOSIS

As we have previously noted the clinical course of schwannomas is benign even though untreated. After complete surgical excision by

enucleation local recurrences do not take place. The well recognized tendency for neurofibromas, especially in von Recklinghausen disease, to undergo sarcomatous changes is not characteristic of schwannomas. In our series, specimens (Cases 4 and 8) harbored areas which showed changes suggestive of malignant transformation (Fig. 5) but all the tumors are clinically and anatomically benign.

Various degrees of malignancy have been reported though rarely among schwannomas. Galek's case, Liberman and Lemos's case are of Stout's cases, and the first case of a series of 6 presented by Manteuffel-Sroog appear to be authentic examples of either recurrent or locally infiltrating types of schwannomas. A feature of genuine schwannoma that is a feature of producing metastasis has been cited in the literature.

ture, with the possible exception of Case 4 in a series of peripheral nerve tumors reported by Cutler and Gross. Their patient had a huge tumor of the arm which showed some of the characteristics of schwannoma. The patient eventually died of pulmonary metastases.

#### END-RESULTS

One patient died 1 year after excision of a schwannoma of the neck following operation for repair of a hernia. The remaining patients are living (from 1 to 6 years following the date of admission) with no evidence of recurrence.

#### SUMMARY

Ten cases of schwannoma in the tissues about the head and neck are described and the first such tumors of the phrenic nerve are reported. In the light of recent evidence, an origin from the cells of Schwann appears to be the most acceptable. This tumor must be differentiated from the neurofibroma, as it is a specific tumor of the sheath of peripheral nerves and possesses distinct anatomic characteristics. In the neck, schwannoma must be differentiated from carotid body tumor in particular, and in the pharynx from lymphosarcomas. Aspiration biopsy permits accurate histological diagnosis. Schwannomas in the head and neck reported in this series were clinically and anatomically benign. They were radioresistant. None recurred following surgical excision.

**NOTE**—Since the conclusion of this study 2 additional cases of schwannoma in the neck were encountered at the Memorial Hospital.

**CASE 11** F. C., white female, 33 years of age, was admitted to the hospital on November 1, 1942, for a painless swelling of the right neck of 14 months' duration. Examination revealed a soft, circumscribed, movable tumor, 3 centimeters in diameter, in the region of the carotid bulb. Aspiration biopsy was not done. At operation an encapsulated tumor was found beneath the internal jugular vein and common carotid artery. This tumor arose from the phrenic nerve, which had to be sacrificed.

**CASE 12** M. C., white female, 39 years of age, was admitted to the hospital on December 5, 1942 for a painless mass in the right neck of 6 weeks' duration. Four years previously the right lobe of the thyroid gland had been removed at the Memorial Hospital because of an adenoma. Examination revealed a firm, movable, ovoid tumor, 1.5 centimeters in diameter, in the region of the carotid bulb. Aspiration biopsy was not done. At operation a spongy, encapsulated nodule was found to arise from the vagus nerve, which had to be severed to make possible removal

of the tumor. So much of the vagus nerve had to be sacrificed that repair of the nerve was not feasible. The post-operative period was characterized by hoarseness, difficulty in swallowing liquids, and paralysis of the right vocal cord, but there has been a steady improvement of these symptoms.

#### REFERENCES

1. ANTONI, N. R. E. Ueber Ruckenmarkstumoren und Neurofibrome. Muenchen J. F. Bergmann, 1920.
2. ASKANAZY, M. Arb. Path. anat. Inst. Tübingen, 1914, 9: 147.
3. BORSCHARDT, M. Beitr. klin. Chir., 1927, 138: 1.
4. COATES, G. M. Arch. Otol., Chic., 1941, 34: 1166.
5. COHEN, M. Arch. Ophth., Chic., 1925, 54: 426.
6. CORNIL and JEANDELIZE. Ann. ocul., Par., 1936, 163: 216.
7. CUTLER, E. C., and GROSS, R. E. Arch. Surg., 1936, 33: 733.
8. ELSCHNIG, A. Arch. Ophth., Chic., 1914, 87: 370.
9. EWING, JAMES. Lectures in Pathology. P. 11. New York: Barnes Press, 1933.
10. FIGI, F. A. Arch. Otol., 1933, 17: 386.
11. FREIFELD, H. Beitr. path. Anat., 1915, 60: 347.
12. FROBOESE, C. Virchows Arch., 1923, 240: 132.
13. GORDON TAYLOR, GORDON. Brit. J. Surg., 1940, 28: 163.
14. GULEKE, N. Arch. klin. Chir., 1926, 142: 478.
15. HOLMGREN, G., and BERGSTRAND, H. Acta otol. Stockh., 1928, 12: 514.
16. KAISERLING, C. Handbuch der speziellen pathologischen Anatomie und Histologie, Henke und Lubarsch, Bd. 4, Hft. 2, 1928, p. 315.
17. KRUMBEIN, C. Virchows Arch., 1925, 255: 309.
18. LANDOLT, LEROUX, J., and MAWAS, J. Ann. ocul., Par., 1925, 162: 209.
19. LHERMITTE, J., and LEROUX, R. Bull. Ass. fr. cancer, 1920, 9: 112.
20. MALLORY, E. J. J. Med. Res., 1920, 4: 349.
21. MANTEUFFEL-SZOELCE, L. Bull. Ass. fr. cancer, 1939, 28: 860.
22. MASSON, P. Am. J. Path., 1932, 8: 367.
23. MAYO, C. W., and BARBER, K. W. Surg. Gyn. Obst., 1934, 59: 671.
24. MURRAY, M. G., and STOUT, A. P. Am. J. Path., 1940, 16: 41.
25. Ibid., 1942, 18: 585.
26. PENFIELD, W. Surg. Gyn. Obst., 1927, 45: 178.
27. RODRIGUEZ, ECANA, and KAPLAN, L. Bol. Acad. argent. cir., 1941, 25: 967.
28. RODRIGUEZ, VILLEGAS, and DANIEL, C. S. Bol. Soc. cir. B. Aires, 1934, 18: 531.
29. ROTINO, A., and KELLY, A. S. Arch. Ophth., 1941, 26: 478.
30. SEIDEL, C. Arch. Ohr. & c. Heilk., 1940, 148: 2100.
31. SEKIGUCHI, S., and OIJE, T. Arch. klin. Chir., 1926, 143: 113.
32. SOUCHANEK. Mschr. Ohrenh., Wien, 1925, 59: 613.
33. STOUT, A. P. Am. J. Cancer, 1935, 24: 751.
34. VAIL, H. H. Ann. Otol. Rhinol., 1933, 42: 476.
35. VEROCA, J. Multiple Geschwuelste als Systemerkrankung am nervoesen Apparate, Festschrift fuer Chari, Wein und Leipzig, 1908, p. 378.
36. Idem. Beitr. path. Anat., 1910, 48: 1.

\*Reported by courtesy of Dr. George T. Pack.



# SULFADIAZINE TREATMENT OF BURNS

## A Comparative Study

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THE successful reports regarding the use of sulfonamides locally in fresh wounds has stimulated certain workers to employ sulfadiazine as a spray in the treatment of burns. The excellent results of Pickrell have shown that sulfadiazine is similar to tannic acid in the treatment of burns with the added advantage of being bactericidal and producing an eschar which is flexible, transparent, and has less tendency to crack.

At the Cook County Hospital we have for years used, in the treatment of burns, various local therapeutic agents including tannic acid (R No. I), trimetaphenol solution (R No. II), gentian violet jelly (R No. III), ether soap (R No. IV) etc. In recent years, the Koch treatment has proved to be particularly advantageous. Although the results secured with these agents have been more or less favorable it has always been our hope that new measures might tend to improve results. With our Nation at war many burn casualties are to be expected, and therefore particularly pertinent at this time is a study such as this by making a comparative study of results obtained with the older measures and those obtained with the recently introduced sulfadiazine spray. An attempt has been made to determine which is the best local therapeutic agent to use in treating burns.

In our study we divided the cases into 3 groups. In the first group we used sulfadiazine spray on the entire burned surfaces. In the second group of cases we subdivided the burned surfaces and used sulfadiazine spray on one half of the burned area and nonadherent pressure dressings on the remaining half. We believed that by using the two methods of treatment in the same individual we would eliminate the personal factor of healing and undoubtedly would have a more accurate comparative study. The fact that each burned area was of the same degree, extent, and duration and that

each area received the same preliminary cleansing with soap and water allowed us to make definite deductions as to the advantages and disadvantages of each method.

### PROCEDURE

On admission to the hospital, each patient with burns was rapidly examined and the cause of the burn, the length of time that had elapsed since injury, and the degree and extent of the burn were established. On a prepared chart, the extent and degree of the burn was indicated for future reference. On the back of these charts all other information was given.

Following recovery from primary shock, the local treatment of each patient consisted of careful aseptic soap and water cleansing with debridement of the burn, under morphine sedation. The burn was then divided into approximately equal portions, in 5 instances, and half treated with sulfadiazine spray while the rest was treated with xeroform and pressure dressings. Sulfadiazine (3 per cent in triethanolamine) was sprayed onto the burned area with an atomizer (as suggested by Pickrell) every hour the first day, every 2 hours the second, every 3 hours the third, and, if necessary, every 4 hours the fourth. During this time the burned area was protected by sterile sheets beneath a heat cradle. In most cases a satisfactory eschar was produced by the third day.

White soap, sterile water and cotton pledgets were used to cleanse the burn to prevent further damage to delicate surface cells.

When infection was absent, the eschar would loosen and separate spontaneously in about 10 to 14 days. Saline compresses after 14 days will precipitate its separation. Sedation with morphine sulfate or phenobarbital as required in most cases to maintain comfort of patient.

Koch's nonadherent pressure dressing used on the remaining half of the burn consisted of the following layers: (1) 3 per cent xeroform in petrolatum base, impregnated in fine mesh gauze (2)

From the Departments of Therapeutics and Surgery, Cook County Hospital, Chicago. This study, as made possible in part by grant from the Lederle Laboratories, Inc.

Sulfadiazine (sulfamidoazopyrimidine) 0.3 per cent triethanolamine 3 per cent sodium benzoate 0.1 per cent water sufficient to make 100 per cent.

During the cleansing process, doctors, trained for 75 to 100 years and there were eyes, mouths, and noses had to be kept open.



or doctor making the application, as well as from organisms normally present in air. Complete asepsis is extremely difficult to maintain throughout the 72 hours required for eschar formation, in spite of proper masking, sterile sheets, etc.

Xeroform pressure dressings, on the other hand, require only *one* application of an easily applied sterile dressing through which reinfection is difficult. This is strictly in accord with Orr's principles in the treatment of compound fractures that is, decrease the incidence of reinfection by decreasing the frequency of dressings. Like Orr's treatment Koch's principles apply to burn therapy—rest, pressure, and drainage.

A comparison of the degree of primary healing was very much in favor of the nonadherent pressure dressing type of treatment. The term nonadherent signifies that no superficial cells are damaged during the application of the dressing and also that the viability of the cells are unhindered during its removal, since nothing adheres to the dressing nothing is pulled off. As a result, the incidence of healing (new skin formation in a second degree burn or clean granulation in third degree) with the nonadherent dressing was approximately 80 per cent whereas, with sulfadiazine, it was only 50 per cent. We believed that this was due to certain deficiencies of the eschar in the sulfadiazine type of treatment which holds true for any type of eschar producing agent. These deficiencies may be summarized as follows:

Eschars require time to cover completely the burned area during this time reinfection occurs with resultant damage to the skin elements.

1. Eschars do some damage to the epithelial cells because of their property of protein coagulation as well as their tendency to adhere to the surface.

2. The accumulation of serum beneath the eschar forms a good culture medium in which organisms may grow.

3. This reinfection beneath the eschar may account for the transformation of some burns of second degree into those of third degree. The absence of pressure increases the plasma loss with its resultant hypoproteinemia, tissue edema, and poor healing.

4. Eschars have a tendency to crack or curl at the edges thus leaving portal of entry for infection.

The last comparison that was made was ease of removal of the various agents. Sulfadiazine proved to be difficult, painful, and tedious in its removal, while on the contrary xeroform was capable of being removed traumatically painlessly and quickly.

#### SUMMARY AND CONCLUSIONS

A comparative study was made between sulfadiazine spray and nonadherent pressure dressing treatment of burns with the following results:

Although sulfadiazine presumably has the bactericidal properties of other sulfonamides, its application as a spray has all the disadvantages of other eschar forming agents, namely reinfection frequently results, healing is incomplete second degree burns may be transformed into those of third degree. It is more difficult and painful to apply and more difficult to remove than the nonadherent pressure dressing.

1. This study served to demonstrate again the advantages of nonadherent pressure dressing as compared to the eschar type of burn treatment because its application, as well as its removal, is easy, quick, and painless. It required less surgery care, showed lower incidence of infection, greater degree of healing, no evidence of toxic absorption, affords greater comfort to the patient. In addition it is a good preliminary treatment in case of deep burns in which grafting is necessary since a minimum of time is necessary before grafting can be done. No time is lost in grafting because the use of pressure and the fine mesh gauze result in a good bed for the graft.

2. The combination of a chemotherapeutic agent applied as a nonadherent pressure dressing might be the procedure of choice because it would have not only the bactericidal effect of the sulfonamide but as well all the advantages of a nonadherent pressure type of dressing.

3. Regardless of the local treatment, the surgical principles so frequently advocated by Koch must be applied if successful burn treatment is to be expected, namely convert all burns from contaminated wounds to clean wounds by aseptic and traumatic cleansing with soap and water, and close the clean wounds and keep them clean and clean until healing occurs.

4. Our discussion of the local treatment of burns should not mask the importance of proper general management of primary shock, hemorrhage, tetanus, and sepsis.

Shortly after completion of this study we read the paper by M. Rothman and associates, on the treatment of burns with 5 per cent sulfadiazine in 8 per cent trypsin-bovine solution. Possibly in larger series of cases our results with sulfadiazine spray would have been more favorable.

#### REFERENCES

1. HARRIS, HENRY. *The Treatment of Burns*, Ed. 1. Am. M. Ass., Cleveland, June 2-5, 1941.
2. KOCH, SCOTTER L. *Surg. Gyn. Obst.*, 1934, May.
3. PICKRELL, KENNETH T. *Bull. Johns Hopkins Hosp.*, 94 August.
4. ROTHMAN, M. et al. *J. Am. M. Ass.*, 1942, 11.

# A NEW NEEDLE FOR THE TREATMENT OF SHOCK BY STERNAL INFUSION

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COMBATING shock is a major problem facing medical officers in the field of battle. Whether the shock is due to trauma of gunshot, shrapnel, or bayonet wounds, concussion, burns, or hemorrhage, early treatment and breaking up of the "Cycle of Death" as described by Moon, is of extreme importance. The introduction of plasma or the albumin fraction of plasma into the circulation, and the use of oxygen and adrenal cortex extract are the most effective means of meeting the problem that have been discovered to date.

The work of Kendrick and Newhouser in making plasma prepared from blood donated through the American Red Cross available for use in the field of operations, has undoubtedly saved many lives by preventing shock from progressing to an irreversible stage in many of the battle casualties. The standard Army-Navy package of dried human plasma is now packaged with water, tubing, and needles necessary for restoring it, and administering it intravenously.

Because of the underlying pathological changes that take place in shock, it is of the utmost importance that the fluid used in combating it be given into the circulatory system. The increased endothelial permeability, which is part of the picture, has caused loss of fluids into the tissues outside of the vessels, with consequent hemoconcentration, reduced blood volume, and reduced volume flow, and plasma or albumin solutions given outside the vascular system cannot be expected to help. The collapse of peripheral vessels, and the stigmation of blood flow in the veins make the intravenous administration of fluids difficult and practically impossible at times when the need is most urgent. Locantini, O'Neill, and Price have shown the feasibility of injection into the marrow cavity in order to reach the general circulation in these cases, and, in adults, the sternum has been selected as the site of choice.

The advantages of reaching the circulation by this route are many. The sternum is easily punctured with a properly designed needle. Once the needle is in place there is no doubt of the fact that the fluid is entering the circulatory system. Movement by, and of, the patient do not dislodge

the needle easily, as is often the case when it is in a thin walled arm vein. Also, concentrated plasma or albumin can be injected forcibly, with no fear of rupturing the vein and wasting the material in surrounding tissues. Taxon and Churchill, in describing the treatment of the burns resulting from the Coconut Grove fire in Boston, mention the difficulty encountered in giving intravenous plasma, and deplore the fact that materials for intrasternal administration were not at hand. Chilcott at St Francis hospital in Evanston, Illinois, being unable to keep a needle in the vein of a severely burned patient, gave 12 units of plasma through one sternal puncture, with recovery.

After over 1700 diagnostic sternal punctures done at the University of Illinois, College of Medicine, and the Cook County hospital in Chicago and after talking to Lieutenant Colonel Douglas B. Kendrick, Jr., at the Army Medical Center in Washington, D. C., and using the needles available for the purpose there, the writer designed a needle which he believes is better and more easily used for sternal puncture and fluid administration than is any other available at present (Figs. 1 and 2).

This needle is simple and can be made cheaply in large numbers for inclusion in plasma and albumin packages for use by the Army and Navy in combat and other zones. The flange on the hub makes it easier to apply the pressure necessary to penetrate the anterior plate of the sternum and also prevents slipping of the fingers and possible contamination of the point of the needle. The knurling of the hub permits easy rotation of the needle in penetrating the bone. The simple lock which holds the stylet in place prevents its displacement and blocking of the needle by a particle of bone.

The following technique may be used in administering fluids intrasternally. The plasma, albumin, blood, or other fluids are made ready to be given. The site for administration, usually the manubrium or the body of the sternum opposite the 2d or 3d interpace, is chosen and the overlying skin is cleared with iodine and alcohol or an acetone-alcohol-mercuric mixture. The skin and underlying tissues down to the sternum are



Fig. 1. Photograph of needle for administering plasma and fluid.

anesthetized with procaine. The needle is inserted through the skin down to the bone in the midline. Then, with the point toward the head, and at an angle of about 45 degrees with the sternum, the needle is forced into the marrow cavity with pressure and a rotary boring motion. The entrance into the cavity is usually indicated by a distinct lessening of resistance as the anterior plate of the sternum is penetrated. Then, to check the presence of the needle point in the marrow cavity and possibly to open up sinusoids and allow more rapid flow of fluids, the stylet is removed, and rapid aspiration with a 5 or 1 cubic centimeter syringe is attempted. When the needle is in place in the cavity there will be a gush of blood and marrow into the syringe, and from 1 to 2 cubic centimeters should be withdrawn. Following this the fluid can be administered either by drip or if speed is urgent by forcible syringe injection. Because of the coagulability of marrow if there is any delay between the above aspiration and fluid administration, the stylet should be replaced to prevent clotting in the needle, and occasionally it may be necessary to inject about 20 cubic



Fig. 2. Needle assembled. Not shown on tub and knurled.

centimeters of physiological saline by syringe to start the flow when the drip method is used. When large quantities of fluids are given over a long period of time it is well to remember that the velocity of flow sometimes tends to increase with time, and that this increase should be controlled to prevent circulatory embarrassment.

Using the above method with the needle suggested, medical officers of the Post Hospital and the 57th Evacuation Hospital at Camp Breckinridge, Kentucky, with no previous experience with sternal punctures, have had no difficulty with the administration of fluids.

Because of the ease with which it can be used and manufactured, it is believed that the needle described for use in the intrasternal administration of fluids would be a valuable aid in the treatment of shock in the combat zone and other civilian emergencies.

#### REFERENCES

1. CARLSON, L. H. Personal communication to author.
2. FAYON, N. W. and CARACALLI, E. D. *J. Am. M. Ass.*, 94, 300, 1929.
3. KENNEDY, D. B. and NEWBORN, L. R. *M. Surg.*, 94, 900, 1926.
4. MOORE, V. H. *Shock—Its Dynamics, Occurrence, and Management*. Philadelphia: Lea & Febiger, 1932.
5. TOCANTINS, L. M., O'NEILL, J. F. and PRICE, C. E. *Ann. Surg.*, 94, 4, 1931.

# A STUDY OF EXTRACELLULAR WATER CHANGES IN PREGNANCY

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**S**TANDER and Pastore write "The weight gain during pregnancy is out of proportion to the weight of the products of conception, which approximately account for one third of the total gain. This excess is undoubtedly mainly due to fluid retention not only in the circulation but also in the tissues. This would indicate that approximately 16 per cent weight increase over the nonpregnant weight is due to fluid. Experiments have already shown that there is about 20 per cent dilution of blood due to hydremia, and it is reasonable to assume that there is an equivalent dilution of the tissue fluids." Observations consonant with this supposition are (a) the marked postpartum diuresis, (b) the simultaneous rapid weight loss in the early puerperium, and (c) the atonic and flaccid condition of the tissues after the diuresis (discharge of edema water).

Beck, on the other hand, writes that practically all of the weight gain, over and above that represented in the conception product is to be accounted for by maternal fat.

The water retention of pregnancy has not been investigated extensively, except for studies of blood dilution and of blood volume increase. Analyses of weight gain in pregnancy are obviously nonspecific.

Unfortunately, there is not available a method for the measurement of total body water. However, there are means of determining the *extracellular* water, at least roughly. It is uncertain whether the water increase in normal pregnancy is confined to the extracellular space. *Extracellular* water, however, does make up at least  $\frac{1}{3}$  of the total body water, and even occult edema frequently shows up as a marked increase in this extracellular water. Measurements of extracellular water, then, show promise of yielding some information about water retention in pregnancy.

In the present paper are reported the results of repeated measurements of the thiocyanate-available water (roughly equivalent to extracellular water) in a large series of patients. Changes in available water are correlated with weight changes, and an attempt is made to account for the increments in and disposition of the water.

From the Margaret Hague Maternity Hospital

## MATERIAL AND METHODS

The total number of patients studied was 442. These were in 2 groups.

1 Sixty-seven patients were taken at random from the antepartum clinic, the only selection being for patients early in pregnancy who were distributed over a wide range of body weights. Measurements of thiocyanate available water were made on the day of selection and were repeated at 32 to 35 weeks of pregnancy. In a few cases third measurements were made antepartum.

2 For a time, all clinic patients were routinely given the test at the 31st to 33d week, and repeated at the 35th to 37th week of pregnancy. These patients, totaling 375, are included in the present study. A few of these had third tests at term.

The patients were given 1000 milligrams of sodium thiocyanate by mouth and were instructed to save all urine until the following morning (average 21 hours later) when the urine collection was completed and a blood sample was taken. The urinary loss of thiocyanate was measured.

Thiocyanate was determined in duplicate in serum and urine by a method described elsewhere (Chesley). Completeness of urine collection was checked by measurement of the creatinine excretion, by the method of Folin (Peters and Van Slyke). When considerable volumes of urine obviously had been lost, the test was discarded.

The thiocyanate available water was calculated by dividing the serum concentration of thiocyanate into the amount of thiocyanate left in the body (i.e. 1000 mgm — urinary excretion). The quotient thus obtained represents the volume of water in which the thiocyanate is distributed. With minor reservations, the water so measured is extracellular (Chesley and Chesley, 1941).

## RESULTS

*Available water gain up to 34th week of gestation*  
At the time of the first measurement of available water, 10 patients were in the first trimester of pregnancy and 57 were in the second. Of these latter, 40 were less than 20 weeks pregnant. The average time in pregnancy at which the test was first done in these 67 patients was 18 weeks. In all cases, the test was repeated at the 32d to 36th

(average 34th) week. Over this interval of 16 weeks (average) the mean rate of available water gain was 208 milliliters per week. In the 10 patients first done at 11½ weeks (average) the mean rate of water gain over a 22 week period was 201 milliliters per week.

We (6-7) have previously found that about ½ of patients in the last 6 weeks of pregnancy will have abnormally high values for a "available water" i.e. edema—frank or occult—is present. Such patients may be considered to have gained more than the normal amount of available water because (1) their volumes of available water are considerably greater than the average normal (2) they very frequently show edema (3) a high proportion develop the pre-eclamptic syndrome and (4) they show an unusually large loss of available water in the first 6 days postpartum.

Of the 67 patients studied 14, or 20.9 per cent, had gained so much water between the first and second tests as to fall into the abnormal range. Of these 4 cases, 8 developed pre-eclampsia. We shall consider these 14 cases separately and shall regard the remaining 53 patients as having gained normal amounts of available water. For these normal patients the average rate of gain in available water was 157 milliliters per week. Six showed a gain of 0 to 50 milliliters, 5 a gain of 51 to 100 milliliters, 16, of 101 to 150 milliliters, 12 of 151 to 200 milliliters, 9, of 201 to 250 milliliters, 3 of 251 to 300 milliliters and 2 of 301 and more milliliters. The mean was 157 milliliters standard deviation, 75 milliliters mode 136.3 milliliters median, 150 milliliters.

It would seem reasonable to suppose that the rate of water retention accelerates as pregnancy progresses. In order to determine whether this occurs, the data for the 53 normal patients have been further analyzed. (1) In the 7 patients first measured at about 11½ weeks the average rate of water gain is 34 milliliters per week, perhaps indicating a slightly lower rate of gain in the earlier weeks of pregnancy. (2) When the second measurement of available water was made at or before the 33d week, the average gain was 145 milliliters per week. In patients whose second measurement was made at 34, 35, or 36 weeks, the average gain was 164 milliliters. This might point to an increasing rate of water gain in these later weeks. While these differences in rate of gain seem slight, it must be remembered that they are minimized by the long interval between tests (average 6 weeks). The differences in total water gained are quite definite.

Comparing the weight gain with the water gain in the 53 normal patients, we find that the average

weight gain was 6.67 kilograms, with an average available water gain of 2.51 kilograms. Thus the available water added accounts for 38 per cent of the weight increment.

In the 14 patients who had abnormally high proportions of available water in the second test at the 32d to 36th week, the average rate of gain in water was 402 milliliters per week—two and a half times that in the normal patients. The average weight gain was 8.17 kilograms, and the available water added made up 77 per cent of the weight increment.

If we assume that the average normal rate of available water gain is about 150 milliliters per week for the first 34 weeks, then at the end of that time the total increment would be 5,100 milliliters. With certain reasonable assumptions as to the status at 34 weeks, this can be accounted for as follows: (1) The fetus weighs about 3000 grams (Stander) and if its available water be 30 per cent, 600 milliliters of the water measured is in the fetus. (2) The amniotic fluid would amount to about 1800 milliliters (Beck). If half of this be included in the measurement of available water (Chesley and Boag) then another 600 milliliters would be accounted for. (3) The uterus may have gained as much as 1000 grams (assumed from uterine weights given by Reynolds). Perhaps as much as 300 milliliters of available water would be found here. (4) The increase in blood volume occurring during pregnancy reaches its maximum at about the 34th week. Taking the data of Thomson and associates which show a gain of 20 milliliters of blood per kilogram of weight, and applying them to a 60 kilogram patient who gains 6 kilograms up to this time the increase in blood volume would be 1740 milliliters. Using the 87 per cent water content of blood in late pregnancy as found by Oberst and Mann, this volume of blood would contain 1440 milliliters of water which is included in the measurement of available water. (5) Finally Goodenit and Lewis have found that a decrease in serum proteins of 1 gram per 100 milliliters will result in an increase in available water amounting to  $3.8 \pm 0.8$  per cent of the body weight. Many writers have found that in pregnancy the serum proteins do decrease but just about 1 gram per 100 milliliters (Stander). In a 66 kilogram patient, this factor might then account for an available water increment of about 500 milliliters. These expected increments total 5400 milliliters, as compared with the amount of 5100 milliliters obtained by calculation from the average measured rate of gain.

Available water gain after the 34th week. Since the volume of available water in late pregnancy

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TABLE I—THE DISTRIBUTION OF RATES OF LOSS AND GAIN IN AVAILABLE WATER IN LATE PREGNANCY

Rate of change in water—ml per wk

Loss

301+  
201-300  
101-100  
0-100

Gain

0-100  
101-200  
201-300  
301-400  
401-500  
501-600  
601-700  
701-800  
801-900  
901+

Cases

9  
7  
10  
27

34

56

58

62

43

20

17

9

4

10

Mean 263 ml. Standard deviation 316 ml. Mode 267 ml. Median 260 ml.  
\*The three groups between 100 and 400 ml were combined for this calculation, since the numbers of cases in each group were nearly the same.

TABLE II—THE AVERAGE RATE OF GAIN IN AVAILABLE WATER IN THE LAST WEEKS OF PREGNANCY

Time of sec ond test	34 or 35 weeks	36 or 37 weeks	38 or 39 weeks	40 or more weeks
Cases	80	217	65	9
Time of first test—wks	Average gain in available water in milliliters per week			
30	141	244		
31 or 32	315	277	02	
33 or 34		113	13	107
35 or 36			10	240

in the last 3 or 4 weeks of pregnancy. Of the 56 patients whose available water was measured after the 34th week, and remeasured in the 38th week or later, 16, or 28.6 per cent, lost water between tests. Perhaps this loss of water is correlated with the well known weight loss which often occurs as labor impends.

Since Stander and Pastore suggested that the water gain in pregnancy should total about 16 per cent of the nonpregnant weight, it is interesting to note that the rate of gain in absolute amounts of available water seems to bear no relation to the body weight (Table III). In this connection, Bray found that the body build did not influence the weight gain, although this has not been uniformly the finding of other writers (see Bray for review).

An approximate estimation of the total gain in available water in pregnancy may be made. It has been calculated here that the gain up to the 34th week might be about 5,100 milliliters. The average gain after this time is about 210 milliliters per week (average of the four lower right boxes in Table III). Thus the total water gain would be about 6,300 milliliters. Of this perhaps 1500 to 2000 milliliters, as measured, are to be found in the fetus, placenta, and amniotic fluid, leaving 4,300 to 4,800 milliliters for hydration of the maternal tissues. Roughly, this would represent an average of 9 to 10½ pounds of the mother's

TABLE III—THE AVERAGE RATE OF GAIN OF AVAILABLE WATER IN LATE PREGNANCY, DISTRIBUTED BY WEIGHT GROUPS

Body weight in pounds	Less than 120	121-140	141-160	161-200	More than 201
Cases	21	117	140	86	11
Average gain per week in ml	321	249	275	241	311
Proportion of patients losing water %	9.5	18.8	15.0	19.8	0.0

can be greatly modified by the limitation of dietary salt (Chesley and Annitto), only those patients on unrestricted diets will be presented as "normals." This may be further justified by the fact that when such salt restriction was imposed, it was usually because of clinical signs pointing to the possible development of toxemia. An additional 55 patients are not included because their proportions of available water were abnormally high.

In 375 normal patients selected as here indicated, the rate of gain in available water after the 32d week averaged 263 milliliters per week although there was a very wide variation and some patients actually lost water (Table I). This average rate of water gain is almost twice that described for the preceding weeks of pregnancy.

This is of particular interest since at this time (32d week) the blood volume nearly reaches its maximum and shortly thereafter begins to diminish (Thomson et al). Also the serum proteins have passed their minimum point, and the amniotic fluid volume is decreasing (Beck). These factors, which seem to bulk so large in explaining water retention up to this period in pregnancy, would no longer seem to operate in further water retention. After the 32d week the fetus approximately doubles in weight (Stander), thus not much more than 600 milliliters of the added available water is to be found here. Presumably the rest of the water gained contributes to the extracellular hydration of the maternal tissues.

From the data in Table II it appears that the average rate of water gain diminishes somewhat



weight gain. Some of this may be lost in the prelabor weight loss.

*Relation of water gain to weight gain in late pregnancy.* We have shown in a previous paper (7) that there is very little correlation between the gain in available water and the weight increment, especially in the last 10 weeks of pregnancy. In half of the patients studied, the weight of available water added was greater than the increase in body weight. In 9 per cent of all cases the patients lost weight while gaining available water. This might be explained in 2 ways: (1) Possibly the permeability of certain cells increases as pregnancy progresses, so as to admit the thiocyanate thus giving an apparent increase in extracellular water. (2) There may be a shift of intracellular water out into the extracellular space. Such a shift is believed to occur in toxemia (McPhail) and may occur toward the end of normal pregnancy.

#### SUMMARY AND CONCLUSIONS

Repeated measurements of thiocyanate available water (roughly extracellular water) were made in 442 patients at different times in pregnancy ranging from the 8th to 40th week.

There seemed to be a gradually accelerating rate of gain in available water.

The total gain in available water up to the 34th week of gestation averaged about 5 liters. This can be accounted for on the basis of certain factors known to be operative in normal pregnancy.

After the 34th week, there was a greatly increased average rate of available water gain. Practically all of this seemed to represent hydration of the maternal tissues. Such water gain occurred despite the fact that certain factors operative in earlier pregnancy now seemed opposed to further water retention.

In the last weeks of pregnancy many patients lost water. This loss may be correlated with the well known weight loss often occurring just before delivery.

The total gain in available water was calculated to average about 6.3 liters, of which 1.5 to 2.0 liters, as measured, are to be found in the conception product.

Hydration of the maternal tissues appears to occur. The average weight of water thus represented was 9 to 10½ pounds. Some of this must be lost with the prelabor weight loss.

There is not a close correlation between weight gain and available water gain in late pregnancy. In half the cases, the weight of water gained was greater than the weight increment.

#### REFERENCES

- BRICE, A. C. *Obstetrical Practice*, 2nd ed. pp. 98-104. Baltimore: Williams and Wilkins Co., 1936.
- BRICE, F. M. *Am. J. Obst.*, 1935, 35, 801.
- COSGROVE, L. C. *J. Biol. Chem.*, 141, 117-121, 1943.
- COSGROVE, L. C., and ALBERT, J. E. A study of salt restriction and of fluid intake in pre-eclampsia and in patients with water retention. *Am. J. Obst.*, 1943, (in press).
- COSGROVE, L. C., and BOOD, J. Extracellular water changes during delivery and the puerperium. In preparation.
- COSGROVE, L. C., and COSGROVE, E. R. *Am. J. Obst.*, 1941, 81, 976.
- Idem. An analysis of some factors involved in the development of pre-eclampsia, with special reference to measurements of extracellular water in 361 patients. *Am. J. Obst.*, 1941, (in press).
- GORDON, A., and LORR, L. *Am. J. M. Sc.*, 1942, 303, 514.
- McFARLANE, F. L. *West. J. Surg.*, 1936, 47, 304.
- OSBERT, T. W., and FLISSE, E. D. *Am. J. Obst.*, 1941, 81, 6.
- PETTER, J. P., and V. R. H. D. D. *Quantitative Chemical Chemistry*, Vol. II. Methods, p. 477. Baltimore: Williams and Wilkins Co., 1937.
- REYNOLDS, S. R. M. *Physiology of the Uterus*. New York: Paul B. Hoeber Inc., 1935.
- STARR, H. J. *Williams Obstetrics*, 16th ed., pp. 105-106. New York: D. Appleton Century Co., 1941.
- STARR, H. J., and PARTLOW, J. B. *Am. J. Obst.*, 1940, 80, 924.
- THORNTON, E. J., HENNINGER, A., GROSS, J. C., and L. W. R. *Am. J. Obst.*, 1935, 35, 41.

# INTERNAL FIXATION IN INJURIES OF THE ANKLE

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**A**MONG the injuries of the ankle, which are becoming more common as a result of the general speeding up of heavy industry and the popularity of winter sports, is the serious complicated fracture or dislocation that presents a problem in treatment. In these cases the ideal conservative methods fail, not only because it is usually impossible to effect an accurate reduction by manipulation, but because there is no adequate means of external fixation. These injuries, then, fall necessarily into an operative group, requiring open reduction and some form of internal fixation to maintain the corrected position. It is the purpose of this paper to classify those injuries that are operative and to describe methods of reduction and fixation that have proved to be successful. Such operative treatment should be undertaken by only the highly qualified surgeon.

Operative reduction, when indicated, should be carried out as soon as possible, preferably within from 24 to 48 hours after the injury. In the interval, in order to prevent swelling and the formation of blebs, the ankle is kept bandaged, elevated, and immobilized by means of a molded posterior splint of plaster.

## FRACTURE OF THE LOWER END OF THE FIBULA

The lower fibula may be fractured as the result of forcible external rotation of the foot or of turning the foot directly outward on the leg. The astragalus as it twists in the joint mortise and strikes against the edge of the external malleolus is the shearing force that causes the fracture. Such a fracture is the typical injury received in skiing when the point of the ski, turned outward, catches in the snow, and the skier pitches forward, twisting the ankle.

The fracture line is usually oblique from side to side, either running from a point slightly above the top of the astragalus upward and backward for a distance of about 2 inches, or extending as a long fracture line with its center at the joint surface. Operative indications should be recognized in fractures of the lower end of the fibula under the following circumstances: (1) in the short oblique fracture when the fibular end is displaced outward and backward with accompanying widening of the joint mortise, (2) in the long oblique

fracture in which the tibiofibular ligamentous structure is damaged, and the fibular fragment rotated backward and outward with accompanying widening of the joint mortise (Figs 1 and 2), (3) in fractures with irregular serrations of the fragments that preclude alinement by manipulative measures (Fig 3). (An attempt at closed reduction may be made after the ankle has been prepared for operative interference, but it is seldom successful.)

*Technique of operation* An incision is made over the fracture directly in the long axis of the fibula. The fracture cavity is cleaned out. The fracture is reduced, the amount of force necessary to effect reduction being much greater than the size of the fragment and the degree of the displacement would seem to require. A long vitalium screw is introduced through the cortices of the fibula and tibia, the exact direction of the screw depending on whether the outward or the rotary displacement is the offending factor (Figs 4 and 5). A plaster boot is applied with the foot straight and at the right angle to the leg.

## TRIMALLEOLAR FRACTURES

The trimalleolar fracture, consisting of fractures of the posterior tibial surface and both malleoli, presents no problem when the triangular-shaped fragment of the tibia is small in size. On the other hand, when a large fragment is separated which, in turn, disrupts the gliding weight-bearing surface of the tibia, it is difficult to reduce the fracture and to maintain the fragment in the corrected position. The poor end-results in this type of fracture are well known (Fig 6). Disability is particularly marked in women, who are most likely to sustain this fracture, because of the fact that when high heels are worn the weight-bearing line falls through the posterior half of the tibial surface.

Operative reduction with internal fixation is indicated when the posterior tibial fragment includes a quarter or more of the tibial surface. A method that is applicable to fresh trimalleolar fractures is the following.

Under fluoroscopic control and with verification of the position by "spot films," a long, sharply pointed and beveled Steinmann pin is driven into the posterior tibial fragment, to the outer side of



Fig. 1 A fresh fracture of the long oblique type showing the fragment displaced outward and rotated, and the joint ankylosed.

Fig. 2 An unreduced oblique fracture of the fibular end, 5 years after the injury, showing the permanently ankylosed joint. Patient still complains of stiffness and pain in the ankle.

Fig. 3 Fracture of the lower end of the fibula with irregular callus formations that preclude reduction by manipulation.

the tendo achillis. The pin is inserted at a slightly upward angle to avoid its slipping when pressure is applied in reducing the fragment. Reduction is accomplished and the fragment held in position by means of the pin.

A short incision is made on the anterior surface of the tibia internal to the anterior tibial tendon and at the best level for the insertion of a screw. Small drill holes are made through the lower tibial shaft and the posterior fragment, the tibia being drilled first at a point determined by the size of the fragment. If there is an question as to whether the fragment has been drilled properly fluoroscopic visualization in two diameters is advisable. A screw is then introduced. In order to permit close approximation of the posterior fragment the screw used should be one shouldered

near the head, or the drill hole in the anterior cortex should be enlarged to permit setting the screw. As the screw is being tightened, care must be taken to note when the reduction is complete otherwise there is danger of stripping the bone threads by continuing the tightening process.

The fracture is then treated as one of the Potts type and if possible reduction is accomplished by the routine manipulative method. When the fracture is of the irreducible type the anterior tibial incision is enlarged, and the reduction is



Fig. 4 Reduction of the long oblique fracture shown in Figure 1.



Fig. 5 Reduction of the fracture shown in Figure 3.

completed according to the technique that is described under the section on Pott's fracture

A molded plaster shell, or a circular cast, is applied with the foot in the position of inversion and at the right angle to the leg (Fig 7, a, b, c, and d)

#### FRACTURE OF THE ANTERIOR TIBIAL SURFACE

A fracture of the anterior weight-bearing surface of the tibia similar to that of the posterior surface, in which a wedge-shaped fragment is broken off and the foot displaced forward, requires operative reduction. Particular care must be taken in handling this fracture, which is practically always of the comminuted type (Fig 8, a and b)

*Technique of operation* An incision of sufficient length to provide ample exposure for inspection is made on the anterior surface of the tibia, internal to the anterior tibial tendon. A long pointed Steinmann pin is driven into the anterior fragment, by means of which it is manipulated into position and maintained while drill holes are being made. A small drill hole is first made through the fragment, its site being determined by the size and displacement of the fragment, and then a drill hole is made through the lower tibial shaft. A screw is inserted and tightened. A plaster boot is applied in either one or two sections, depending on the amount of swelling that may be expected. If the comminution is extensive, the foot should be immobilized in the position of slight toe-drop in order that the weight-bearing line will lie backward and thus facilitate early use

#### FRACTURE OF THE INTERNAL MALLEOLUS

Occasionally in an isolated fracture at the base of the internal malleolus, an obstacle to closed



Fig 6 A typical poor end result from conservative treatment of a trimalleolar fracture, showing displacement of the posterior fragment and arthritic changes

reduction is presented by a curtain of soft tissue that is interposed between the tibia and the fractured malleolar surface (Fig 9). If such a fracture is not accurately reduced, a fibrous union takes place, causing the area to be tender and painful and the joint mortise to be unstable.

Operative interference is required to release the fragment from the tight offending curtain of periosteum and the ligamentous band. Once the fragment has been freed, it is surprising with what ease the reduction is accomplished and the



Fig 7 Roentgenograms showing a, a fresh trimalleolar fracture, b, the Steinmann pin and screw in place, c, the

screw alone in position, d, the end result 7 months after reduction



Fig. 8. a, left, Comminuted fracture of the anterior tibial surface with forward displacement of the foot. b, reduction and fixation of the fragment by screw.

corrected position maintained. Following the reduction, the malleolar fragment is fixed to the tibia by means of a chromic catgut suture, which is first carried around the fragment and then passed through a drill hole in the tibia. A plaster boot is applied with the foot in the position of slight varus and at the right angle to the leg.

#### POTT'S FRACTURE

One obstacle to the reduction of a Pott's fracture by the routine manipulative method is the



Fig. 9. A fracture of the lateral malleolus irreducible by manipulation because of interposed soft tissue.

interposition of a curtain of soft tissue between the inner malleolar fragment and the tibia. This complication has just been discussed.

Another obstacle to reduction is the dislocated posterior tibial tendon (Figs. 10 a and b and 11). A Pott's fracture that is complicated by this dislocation may be treated as follows:

An incision is made below the inner malleolus. The tibialis posterior tendon is released from between the articular surfaces of the astragalus and the tibia, and the displaced astragalus is reduced.

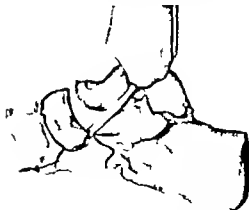


Fig. 10. a, left, Displacement of the posterior tibial tendon under the internal malleolus. Note the locking of the joint mortise. b, Lateral view of the displaced posterior tibial tendon.



Fig 11 An irreducible Pott's fracture due to displacement of the posterior tibial tendon

to its normal position. Torn ligaments are carefully repaired to prevent a recurrent dislocation of the tendon. Following the reduction, a posterior plaster slab and a pressure bandage are applied to hold the foot in the position of slight equinovarus.

#### SEPARATION OF THE TIBIA AND FIBULA

A separation of the tibia and fibula as the result of the tearing of the tibiofibular ligament may occur in conjunction with a fracture in the region of the ankle or as a separate entity. The recognition and treatment of this lesion are important, because of the disability that may ensue from the disrupted relation between the astragalus and the tibia by the widening of the ankle mortise.

Internal fixation is the best form of treatment. A Kirschner wire, cut with threads, is drilled through the tibia and fibula, as near to the joint as possible. The holes in the skin are enlarged to permit the insertion of two ferrules equipped with thumb nuts for tightening (Fig 12). If traction is needed in managing an accompanying fracture, a Braun splint is used, with the ends of the wire serving as attachments for the traction (Fig 13, a and b). The traction splint remains on until union is sufficiently solid to permit the removal of internal fixation and the application of a plaster boot.

#### SEPARATION OF THE LOWER EPIPHYSIS OF THE FIBULA

In this epiphyseal injury, the fragment is rotated backward, with the tip of the fibula acting



Fig 12 Separation of the tibia and fibula, before and after reduction

as a fulcrum, and it occasionally takes with it a jagged spicule of bone from the fibular shaft. Reduction by closed methods is prevented both by the fulcral end of fibula and spicule of bone.

The displacement is easily corrected after operative exposure of the fracture. A chromic catgut suture is used to hold the fragment in position. The ankle is immobilized in a plaster cast with the foot turned a shade inward. Care must be taken not to tilt the fragment outward at the epiphyseal line by inverting the foot too much (Fig 14, a and b).

#### RECURRENT DISLOCATION OF THE PERONEAL TENDONS

Recurrent slipping of a peroneal tendon over the lower end of the tibia is accompanied by an uncomfortable jarring snap from which the patient seeks relief. The underlying pathology in these cases may be lax ligaments, a shallow groove for the tendon, or the presence of a supernumerary tendon that lies farther out beneath the tip of the malleolus than do the other tendons.



Fig 13 a, left Separation of the tibia and fibula associated with comminuted fractures of the tibia and fibula before reduction. b After reduction.



Fig. 4. a, Separation of the lower epiphysis of the fibula, showing back and rotation of the fragment including spicule of bone from the fibular shaft, and forward displacement of the foot. The contour of the epiphyseal line prevents reduction. b, End-result showing practically normal joint.

Operative repair is indicated in recurrent dislocations. In a case in which a supernumerary peroneal tendon was found to be dislocated the following technique was carried out.

An incision was made in the direction of the long axis of the peroneus longus. The superior retinaculum was found to be rudimentary, narrow thin, and ruptured at its attachment to the fibula. An accessory peroneal tendon comparable in size to the peroneus longus, was lying in a shallow groove near the tip of the fibula. To prevent recurrence of the dislocation, this accessory tendon was first attached to the master tendon both above and below the malleolus. The retinaculum was repaired and reinforced by a slip of

the cruciate crural ligament. A plaster boot was applied with the foot at the right angle to the leg and in slight varus (Fig. 15).

The patient was able to resume skiing in the following winter.

#### AFTER-CARE

The secure fixation of the fragments ensured under operative management makes it possible for one to be resumed early thereby materially shortening the convalescent period. Weight bearing is a far more satisfactory means of promoting the return of function than the application of heat and massage, although in the presence of contraindications to weight-bearing physiotherapeutic measures may be used.

As soon as the wound has healed and while the foot is still in the protective dressing, the patient may begin to bear weight with the aid of crutches. Full weight bearing may be resumed in about a week following recurrent dislocation of the peroneal tendon or fractures of the internal malleolus or the lower end of the fibula. In the other types of injuries, full weight bearing is possible at about the 6th week after the injury. If the fractures have been comminuted, full weight bearing should not be attempted for from 6 to 8 weeks.

The screw should be removed in all cases after union is complete. Local anesthesia may be used in this procedure.

#### SUMMARY

The accurate reduction that is essential to the successful treatment of injuries around the ankle cannot be obtained by conservative methods in certain complicated fractures and dislocations. These cases fall necessarily into a group that requires not only open reduction, but also some form of internal fixation. It is important that



Fig. 5. Slipping of supernumerary peroneal tendon, showing the out and flare and flattening of the fibular end due to pressure of the displaced tendon.

operative indications are recognized promptly and that manipulative treatment is avoided

A classification of those injuries that require

operative treatment has been presented, and methods that have given excellent results have been described

## THE ELECTROENCEPHALOGRAMS OF MONKEYS FOLLOWING THE APPLICATION OF MICROCRYSTALLINE SULFONAMIDES TO THE BRAIN

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THE sulfonamides have been proved to have a direct antibacterial action when applied to contaminated and infected wounds in general, and should be of similar value in wounds of the brain if undesirable side effects do not contraindicate their use

A number of histological studies (2, 4, 5, 6, 10, 12, 13) have been reported which show that the crystalline compounds placed on the brain or in brain wounds acted as foreign bodies, caused inflammatory reactions, became encysted, but finally disappeared completely. Nerve cells, myelin sheaths and neuroglia, adjacent to the compounds, showed no changes. The inflammatory reactions produced remained as local ones and lasted only as long as the drugs remained. The intensity and duration of the reactions about the compounds varied only with the amounts applied and the solubility, which influences the rate of disappearance and therefore the duration of the reaction. In treated wounds the late end scarring was no more intense than in comparable wounds in which no drug had been implanted. From the histological studies alone it seemed that the use of sulfonamides in potentially infected or infected wounds of the brain was justifiable, in spite of the transitory reactions, if they were used in moderation.

The first communications suggesting that more circumspection was necessary than the histological studies had demanded, appeared in 1942. Watt and Alexander reported 5 patients who had epileptic seizures following the application of

sulfathiazole to the brain. Pilcher, Angelucci and Meacham pointed out the epileptogenic properties of sulfathiazole when applied to the brain of animals and warned against its use. Naffziger had 1 patient who developed status epilepticus following its use on the brain.

In 1940, Professor Adrian stated that he had carried out electroencephalographic studies on anesthetized rabbits after sulfanilamide and sulfapyridine had been applied to the brain. He found little effect on the electrical activity of the cortex after sulfapyridine and slight depression after sulfanilamide. At this time he had not done experiments with sulfathiazole, and sulfadiazine was not yet available.

The purpose of this communication is to report the effect of the application of sulfanilamide, sulfapyridine, sulfadiazine, and sulfathiazole on the electrical activity of the brain of the unanesthetized monkey, when these various drugs were applied to the surface of the uninjured brain and when injected into severely damaged brain.

### A THE EFFECT OF THE APPLICATION OF SULFONAMIDES TO THE UNINJURED CORTEX

*Experimental procedure.* Four *Macaca mullata* monkeys were used for this experiment, one for each of the drugs to be tested. Microcrystalline preparations of the various sulfonamides were applied to the cortex.

The entire procedure in each of the 4 animals was carried out under aseptic conditions and under local anesthesia with 1% 1500 nupercaine. The monkeys were restrained relatively painlessly in a special holder.

Two holes, 6 millimeters in diameter, were made in the skull about 12 millimeters apart over the motor and sensory areas of each hemisphere.

From the Department of Neurology and Neurosurgery, McGill University and the Montreal Neurological Institute.

This study was carried out with the aid of the Subcommittee on Surgery of the Associate Committee on Medical Research of the National Research Council, Ottawa. Microcrystalline sulfonamides kindly furnished by Smith, Kline & French.



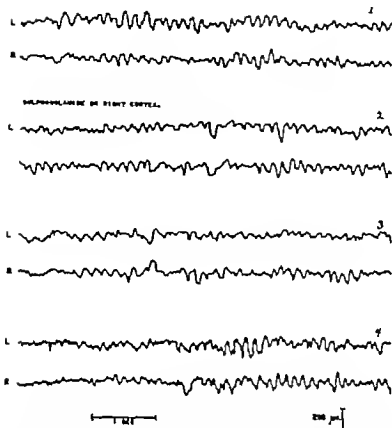


Fig. 1. Electroencephalograms taken with bipolar electrodes from pia arachnoid over uninjured cortex, simultaneous recording from left and right sensory-motor regions. Sulfanilamide macrocrystals are applied on cortex beneath electrodes on right hemisphere. Note absence of appreciable change in sample records (after 5 minutes) 3 (after 20 minutes) and 4 (after 1 hour) compared to the control sample.

The holes were then threaded. A circle of dura was removed under each hole and avascular areas of the pia-arachnoid were pinched in several places with a fine needle with care not to injure the underlying cortex. Then threaded leucite plugs carrying sealed silver electrodes were screwed into the skull and electroencephalographic tracings were taken to serve as control.

When the control record was completed, one plug was removed over the motor area of one hemisphere and a macrocrystalline preparation of one of the sulfonamides to be tested was applied through the dural opening to the surface of the cortex. The plug was immediately replaced and electroencephalographic recording was begun at

once. As well as the control record, before application of the drug the simultaneous recording of the electrical activity of the cortex at any time within the 24 hours this animal was studied (Fig. 1). There was no evidence of even a depression in the amplitude of the normal rhythms. To assure that an adequate amount of the drug had been applied further applications were made after 20

Results of application to uninjured surface of the cortex. 1. Sulfanilamide. There was no change in the electrical activity of the cortex at any time within the 24 hours this animal was studied (Fig. 1). There was no evidence of even a depression in the amplitude of the normal rhythms. To assure that an adequate amount of the drug had been applied further applications were made after 20

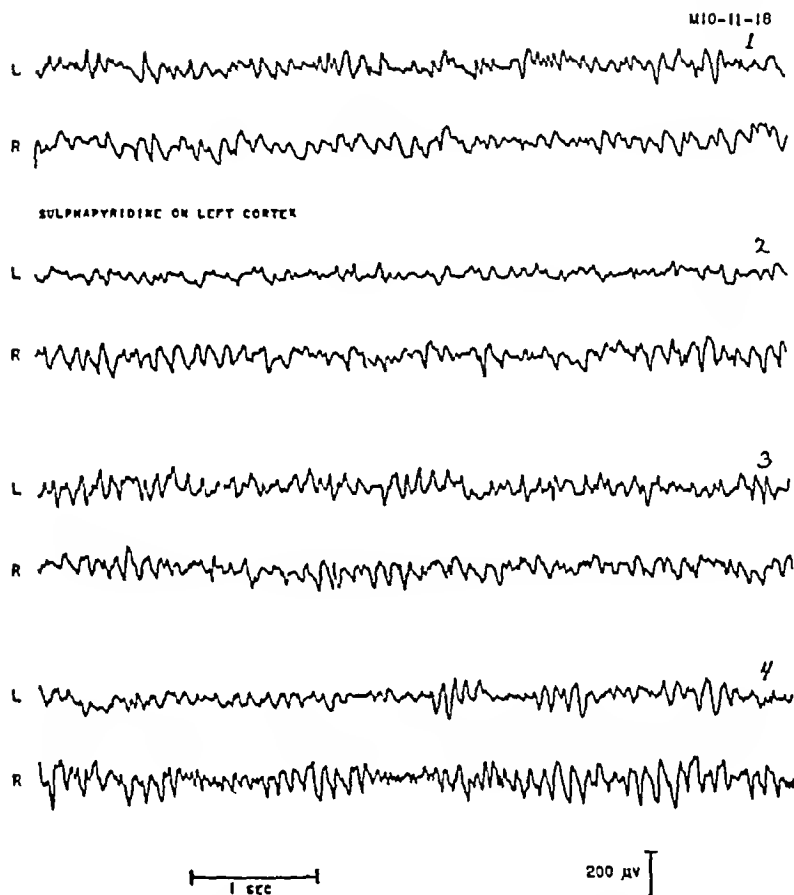


Fig. 2. Electroencephalograms taken with bipolar electrodes from pia arachnoid over uninjured cortex. Sulfapyridine was applied beneath electrodes on the left side. Note absence of change in records 2 (after 4 minutes), 3 (after 2 hours 20 minutes), and 4 (after 21 hours) as compared to control sample 1.

hours, and this time microcrystals of sulfanilamide were placed in larger amounts than used initially beneath each one of the electrodes over the right hemisphere, whereas they had been placed on the cortex under but one initially. Still no change in electrical activity from this region was observed though recordings were carried out at intervals over a period of 4 hours.

The animal did not seem to be much disturbed by the procedure and was allowed to survive for experiments of other types.

**2 Sulfapyridine** During the first 10 to 15 minutes following the application of sulfapyridine there was a slight depression of the normal activity of the cortex as compared with the control from this side and with the opposite cortex. However, the electrogram returned to normal in every

respect within 2 hours (Fig. 2). Perfectly normal electrograms were obtained up to 21 hours after the application, when recording was continued. No slow waves or epileptiform discharges were recorded at any time. There were no clinical signs of cortical disturbance. The animal was released for experiments of a different nature and apparently none the worse for the experiment.

**3 Sulfadiazine** The animal chosen for this experiment had been used 55 days before in an experiment, not included in this report, in which sulfonamides were applied to the wounded brain. He was chosen for the experiment because sulfathiazole had produced not only electroencephalographic evidence of focal seizures but also severe focal and general seizures which had continued at intervals for 1 week, after which time the seizures

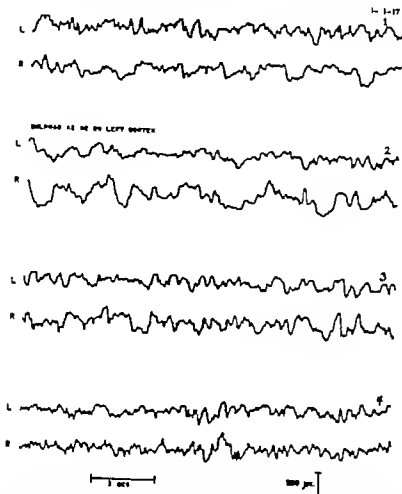


Fig. 3. Electroencephalograms taken with bipolar electrodes from the pial anastomosed, left and right sensory motor regions. Cortex had been injured near the posterior end of the pair of electrodes in previous experiments 55 days before. When this animal had convulsions in response to sulfadiazine. Sulfadiazine as applied beneath the anterior electrode which was over uninjured left motor cortex. There was no appreciable change in the electrogram as illustrated in samples (after seizures) 3 (after 5 hours) and 4 (after 24 hours) — control.

stopped and the electroencephalographic tracings showed evidence of brain damage but no seizure waves. It was felt that the result after sulfadiazine would be doubly significant if negative since the susceptibility to convulsion with sulfathiazole had been demonstrated. The cortical injury had been bilateral. The sulfathiazole had been placed on the right side only.

Two electrodes were placed anterior to the injured cortex on the right and left sides over the

uninjured cortex. The control runs showed some slow wave activity the result of the previous injuries most marked on the right side (Fig. 3).

Following the local application of macrocrystal line sulfadiazine to the uninjured cortex on the left side beneath the most anterior electrode no appreciable change in the electroencephalographic tracing resulted. More drug was then applied, this time to the cortex underneath both electrodes on the left side again with no effect on the trac-

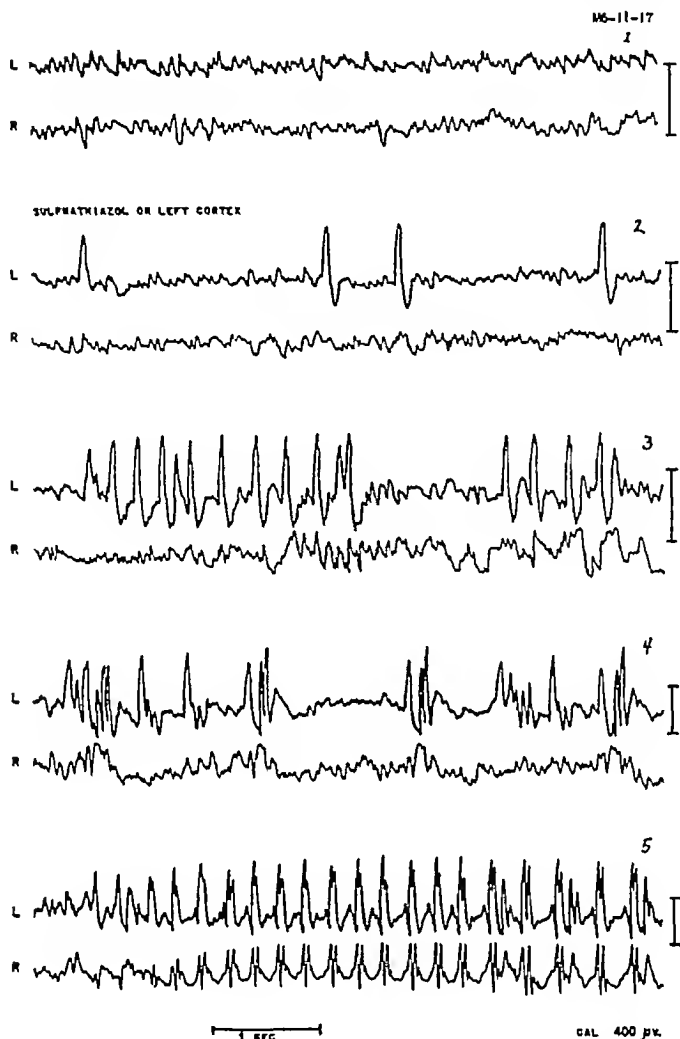


Fig 4 Sulfathiazole applied to the left motor area over uninjured cortex produced large "spike like" waves in 18 minutes as shown in sample 2. In 27 minutes, 3, Jacksonian attacks confined to the right hand and arm were seen to accompany the burst of epileptiform waves in the electroencephalogram. Within 5 hours, sample 5, there was some spread of the seizure to the right hemisphere in the electroencephalogram and the left side of the body was also involved in convulsive movements. Calibrations at right equal 400 microvolts. Note reduction of sensitivity in samples 4 and 5, 1, control.

ings. Recording was continued at intervals over a period of 6 hours and then discontinued and the animal made an uneventful recovery.

4 *Sulfathiazole*. The animal used for this experiment had been used 55 days before for the experiment with sulfadiazine. Cerebral wounds had been produced in the posterior parietal regions

on both sides and microcrystals of sulfadiazine had been injected into the damaged cortex on the right side. No changes in the electroencephalographic tracings of epileptiform nature were recorded, and the animal showed no abnormality in clinical examinations.

The electrodes were placed well anterior of the

area of previous brain damage, and the control records showed little evidence of abnormality and no epileptiform activity.

Eighteen minutes following the application of sulfathiazole, beneath the anterior electrode on the left side, large amplitude, isolated, negative spikes appeared from that area (Fig. 4). The electrical activity from the right homologous region was undisturbed at this time and no clinical seizures were observed. After 25 minutes the epileptiform spikes became larger and were grouped together in bursts. Clonic movements of the right hand began to occur at this time and there also appeared some disturbance in the normal activity of the opposite hemisphere shown by small sharp waves, apparently transmitted from the large spike discharges on the left side. Within 1 hour the bursts of spike activity had become still more frequent and of greater amplitude, and the clinical seizures involving the right hand and arm were more forceful and lasted longer.

After 5 hours the focal seizures which had been limited to the right hand spread to the left side of the body and the attacks were generalized. This was shown in the electroencephalogram by synchronous spikes from the two hemispheres (Fig. 4, sample 5).

The clinical seizures continued for 4 days and then stopped and the animal made a good recovery.

#### SUMMARY

A appreciable change in the electrical activity of the cortex and no signs of cortical damage have been recorded or observed following the local application of microcrystalline sulfanilamide, sulfapyridine or sulfadiazine to the uninjured cortex. Microcrystalline sulfathiazole, however, produced a striking local irritation of the uninjured cortex within 18 minutes of its application. Electroencephalographic evidence of first focal seizures and then general ones have been recorded. Typical Jacksonian seizures and generalized seizures took place. Electroencephalographic evidence and behavior of the animal's seizures showed that the seizure storm always commenced in the area of the cortex to which the drug was applied.

#### B. THE EFFECT OF THE INJECTION OF MICROCRYSTALLINE SULFONAMIDES INTO DAMAGED CEREBRAL TISSUE

*Experimental procedure.* Four monkeys were used for this experiment, 1 for each of the drugs to be tested. Microcrystalline preparations of the various sulfonamides in a suspension made serum isotonic with sodium chloride were injected into traumatized brain. Normal saline solution was

injected into traumatized brain of the opposite hemisphere as a control.

The operative procedures were carried out under rigid aseptic conditions. The placement of leucite plugs carrying electrodes and trephine openings in the skull were made under neonatal anesthesia (0.32 gram of nembutal per kilogram of body weight) given intraperitoneally. Trephine holes, 1 centimeter in diameter, were made in the skull over each parietal lobe. The recording leucite plugs carrying the electrodes were screwed into the skull near the anterior and posterior borders of the trephine openings. The dura was not incised except by accident under one recording electrode in 1 animal. The scalp incisions were closed in layers about the electrodes.

The animals were left for 24 hours to recover from the anesthesia before electroencephalographic recordings were begun. At this time they were feeding and seemed normal.

The recordings were done with the animal restrained in a special holder without anesthesia. Control records were taken from each hemisphere and then with aseptic technique needles were passed through the scalp over the trephine openings and through the dura into the brain for a depth of about 6 millimeters. The needle points were then roughly manipulated with a rotary movement to damage the cortex on each side. One cubic centimeter of normal saline was injected through the needle on the side to be used as a control and 1 cubic centimeter of a 10 per cent suspension of microcrystalline sulfonamides through the needle on the other side. Electrical recordings were begun at once.

1. *Sulfanilic acid.* The electroencephalographic tracings of cortical activity were changed after the brain damage, and by the injection of saline on the one side and sulfanilamide on the other. One minute after the injection, normal rhythms are absent on both sides (Fig. 5). Depression in amplitude of electrical activity was most marked on the side of the sulfanilamide injection and the depression lasted longer on this side. This depression began to disappear in about 2 hours. Within 6 hours the electroencephalograms from the two sides were indistinguishable and no abnormal waves were observed of an epileptiform type; the only abnormal waves present being those characteristic of brain injury. The final electroencephalograms on this animal were taken 24 hours after the injection and the records obtained were essentially the same as those recorded 6 hours after the wounding and the injections.

The conclusion from this experiment then, is that sulfanilamide did not increase the evidence of

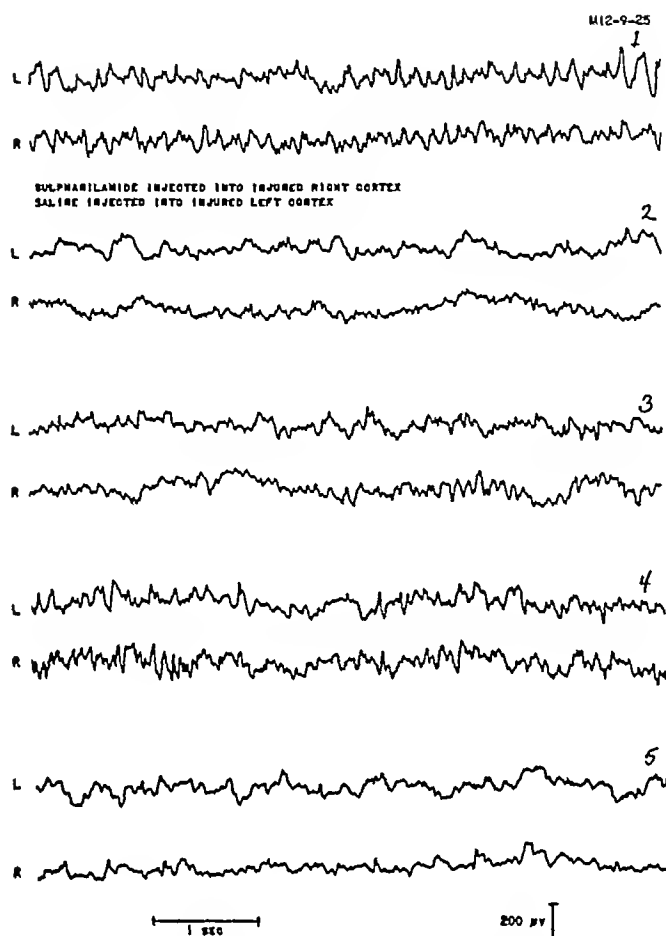


Fig 5 Electroencephalograms before, 1, and after injection of 1 cubic centimeter of 10 per cent suspension of microcrystalline sulfanilamide into injured brain, right parietal area, and control injection of 1 cubic centimeter normal saline into injured left parietal area. Note slight depression in amplitude of electrical activity in samples 2 (after 48 minutes), and 3 (after 2 hours, 8 minutes), but no evidence of excitatory action 4, six hours, 46 minutes, 5, 24 hours

injury, did not cause epileptiform discharges, but did perhaps cause a slight depression in the amplitude of activity for a longer period than did brain injury and normal saline injection. The animal recovered without incident.

**2 Sulfapyridine** Electroencephalograms taken 1 minute following the brain wounding, the injection of saline on the control side, and 1 cubic centimeter of a 10 per cent suspension of microcrystalline sulfapyridine, showed large amplitude, slow continuous waves whose frequencies were between 1 and 2 per second, replacing completely the normal rhythms on the side of the drug injection (Fig 6). There was relatively little imme-

diately change in the right hemisphere which had been wounded and injected with 1 cubic centimeter of normal saline.

After 25 and 30 minutes the slow waves had increased in amplitude from the drug side, and low amplitude slow waves intermingled with normal rhythms from the saline control side.

At 5 hours the tracings began to show some more rapid sharp waves from the drug side.

The records taken 24 hours after the drug showed a few random spikes characteristic of epileptic discharges though they were always moderate in amount and of low amplitude.

Electroencephalograms 6 days, 15 days, and 25

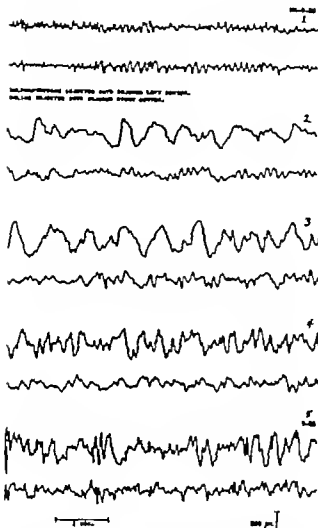


Fig. 6. Electroencephalograms before and after injection of cubic centimeter of 1 per cent suspension of microcrystalline sulfapyridine into the injured left parietal area and control injection of cubic centimeter of normal saline into the injured right parietal area. Large slow waves appeared immediately from drug injected side, sample 1 (after response) and became somewhat epileptiform after 5 hours, sample 5. This does not occur without injury (see Fig. 5) control; 3, after 27 minutes, 4 5 hours, 5 minutes.

days later all showed occasional episodes of moderate amplitude epileptiform activity from the anterior border of the injured sulfapyridine injected hemisphere. There were some low amplitude waves of the same form from the injured saline injected hemisphere. This animal had made an uneventful recovery after the experiment and had never been observed to have clinical seizures.

It was noted at the time of injecting the drug that the injury to the brain produced on this side would probably be greater than on the saline control side. This fact, together with the persistence of abnormal electrical activity 55 days after the injection, indicates that the abnormal discharges were probably due to the wound rather than to sulfapyridine. The 100 milligrams of

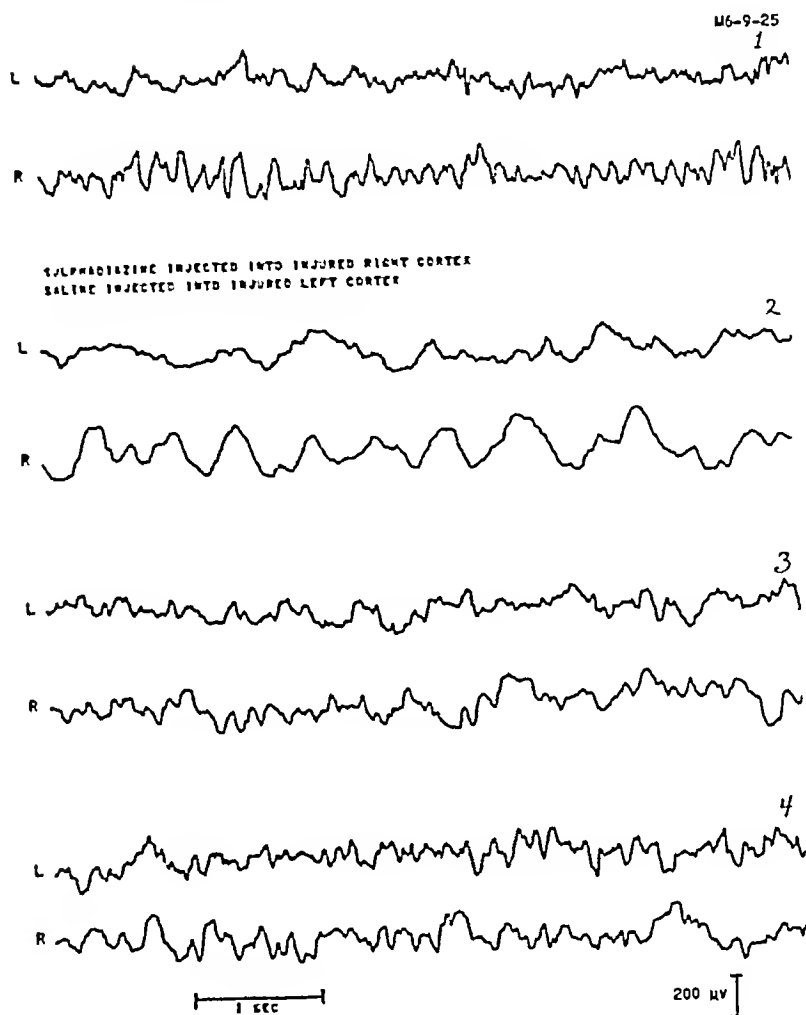


Fig 7. Electroencephalograms before and after injection of 1 cubic centimeter of 10 per cent suspension of microcrystalline sulfadiazine into injured right parietal area and 1 cubic centimeter normal saline into injured left parietal area. Slow waves replaced normal rhythms immediately following injury, more from the drug injected side, sample 2. Results of injury were about equal in samples 3 and 4 taken 2 hours 8 minutes and 13 days following injury. 1, control

sulfapyridine injected would have been expected to be absorbed long before the last tracings were taken. The conclusion that the spike discharges were not due to sulfapyridine, but to the wound alone, is supported by the fact that the direct application of sulfapyridine to the uninjured cortex caused no seizure waves in other experiments.

**3 Sulfadiazine** Within the first half hour after wounding and the injection of 1 cubic centimeter of physiological saline on the control side and 1 cubic centimeter of a 10 per cent suspension of

sulfadiazine on the other side, there was an increase in slow wave activity on the side injected with the drug (right) and to a lesser extent on the control side (left) as shown in the second sample (Fig 7).

After 2 hours the recordings from the drugged side and from the control side were essentially the same, and they remained the same when tested at intervals up to 13 days following the injection.

There were no clinical signs of cerebral disturbance at any time after operation, and it was this animal which was chosen to be used in the experi-





Fig. 8. Electroencephalograms before and after injection of cubic centimeter of 1 per cent suspension of microcrystalline sulfathiazole into injured left parietal area, and injection of cubic centimeter normal saline into injured right parietal area. The right parietal area was accidentally injured before the control record, sample causing random slow waves to appear. Local epileptiform waves from the drug injected side increased in amount during first 5 hours, samples (5 minutes) 3 (44 minutes) and 4 (1 1/2 hour) and 4 day samples, 5 and 6 (there was evidence of transmission of epileptiform activity to the opposite hemisphere, and animal as having generalized convulsions, beginning on the right side. Calibration at right of samples equals 400 microvolts. Note reduction in sensitivity for samples 4 (5 hours, minutes) to 6 (4 days).

ment carried out 55 days later with sulfathiazole on the uninjured cortex.

*Sulf. thiazole.* In this animal an accidental

injury to the brain had been made under one of the recording electrodes as it was being inserted. This caused slow waves to appear in the control

electroencephalographic records taken before the drug was injected. The injury was on the *right* side (first sample of Fig 8). Because of this, the drug was injected into the wound made with the hypodermic needle in the *left* hemisphere. One cubic centimeter of a 10 per cent suspension of microcrystalline sulfathiazole was injected. A similar wound was made with a hypodermic needle on the right side, in spite of the previous accidental wounding, and 1 cubic centimeter of physiological saline was injected into this wound.

Within the first 5 and 10 minutes after the bilateral injuries and the injections, there was a progressive increase in the slow wave activity from both sides. After 15 minutes the amplitude of the electrical activity was increased on the side of the injection of the drug, and a few low amplitude epileptiform spikes appeared. Over the next 20 minutes these isolated spikes increased in amplitude and frequency. Forty minutes after the injection bursts of epileptiform spikes appeared from the left side which were several seconds long (Fig 8, sample 3). The epileptiform activity gradually increased during the first 5 hours from the region where sulfathiazole had been injected. There were no convulsive movements of the animal during the first 5 hours of recording (Fig 8, sample 4), but during the electroencephalographic bursts of spikes the animal's gaze would become fixed and this would be followed by blinking of the eyes (the drug was injected into the posterior parietal region, not near the motor area).

The next morning, 23 hours after the experiment was begun, the animal was having frequent seizures which began in the right hand, spread over the right side and frequently, in the more severe attacks, spread to the left side. Recordings taken at this time showed prolonged episodes of very large amplitude multiple spike discharges from the left hemisphere with some evidence of transmission to the right side (Fig 8, sample 5). Four days later, the animal was still having frequent and severe seizures and records showed the epileptic activity had increased in the left hemisphere and was showing more spread of these waves to the right side where they were, however, of lower amplitude.

The convulsions in this animal continued to increase in severity and as the general condition was deteriorating, the animal was killed 5 days after the drug was injected. The dura was tense, and the convulsions were flattened. This was due to considerable hemorrhage in the brain wounds made with the hypodermic needles on both the right and left sides. The findings were sufficient, it seemed, to account for the unfavorable course

It is not felt that the hemorrhages vitiate the experiment but they do complicate it.

In conclusion sulfonamides act on injured cerebral tissue as they do when applied to the uninjured cerebrum. It was inevitable that the electroencephalograms in the two sets of experiments were not entirely comparable. In the animals with wounds there is evidence of the wounding and also changes as the result of the increased pressure after the injection of the physiological saline on the one side and the suspension of the drug on the other. Sulfathiazole was the only one of the four drugs which produced epileptiform discharge in the electroencephalogram and convulsive seizures in the animal.

#### EVALUATION

One of the most careful and significant articles we have discovered on the antibacterial action of sulfonamides in infected wounds is by Green and Parkin. They point out that the view that different sulfonamides are specific for different organisms is now held to be fallacious. The effect of the different sulfonamides on any species is dependent on the ability of the compound to block enzymes whose substrate is para-aminobenzoic acid. Their mode of *in vitro* activity parallels in most instances their action *in vivo*. The action is directly antibacterial therefore, and it is due to this and not to any direct action on body tissues generally that infection is controlled. *In vitro* tests carried out by these authors have shown that sulfanilamide, sulfapyridine, and sulfathiazole required increasing amounts of para-aminobenzoic acid to block their antibacterial activity. They suggested that a tentative evaluation of the efficiency of the 3 compounds as measured by the *in vitro* test is 1 for sulfanilamide, 5 for sulfapyridine, and 50 for sulfathiazole. They did not carry out *in vitro* tests with sulfadiazine and no reports could be found in the literature permitting the antibacterial activity of sulfadiazine to be evaluated so definitely as the results obtained by Green and Parkin for the other drugs. Spinks' report of *in vitro* studies does show the efficiency of sulfadiazine to be much greater than sulfanilamide and sulfapyridine but less than sulfathiazole.

Since sulfathiazole has been shown to have the greatest *in vitro* power to inhibit bacterial growth, it should therefore be the most potent drug in potentially infected and infected wounds of the brain. Our experiments, however, have provided evidence agreeing with the findings of Pilcher's group and those of Watt and Alexander that sulfathiazole, even in small amounts, may cause convulsive seizures when it is applied to the intact

or wounded cerebral cortex. We have described experiments on 2 monkeys in some detail where electroencephalographic studies of the changes in cortical activity preceding the actual development of clinical seizures have been followed in unanesthetized animals. Actual seizure and electroencephalographic evidence, showing that they have developed from the brain at the site of the application of this drug, have been studied also in cats and still other monkeys. While clinical seizures have not occurred following the application in every experimental animal, electroencephalograms have always shown either excitation or epileptiform waves.

The solubility of sulfathiazole in serum at 37 degrees centigrade is given as 84 milligrams per cent by Lyons and Burbank. Because sulfathiazole altered brain waves in such a relatively short time after its application to the brain, it seemed that the effect might occur at much lower concentrations than maximum saturation. If this impression were correct nerve cells might be exposed by intravenous injections of sulfathiazole blood levels which would irritate and even cause seizures.

In 2 monkeys, without anesthesia, convulsions were produced by the intravenous injection of the sodium salt of sulfathiazole. Electroencephalographic records were taken before and during successive injections, and samples of blood were taken at intervals for the determination of blood concentration.

In the first experiment, facilitation of cortical discharge was apparent in the electroencephalogram when the blood level reached 18 milligrams per cent of free and 25 milligrams per cent total sulfathiazole. However it was not until the blood levels reached 84 milligrams per cent free and 110 milligrams per cent total that a sudden burst of large epileptiform waves appeared in the electroencephalogram and the animal had a major convulsive seizure. The animal then went rapidly into severe status epilepticus.

In the second monkey the first evidence of cortical facilitation appeared in the electroencephalogram when the blood levels were 37 milligrams per cent free and 50 milligrams per cent total respectively. Again marked epileptiform discharge with convulsions did not appear until very high blood levels were reached, 80 milligrams per cent free and 123 milligrams per cent total, respectively.

From these 2 experiments on unanesthetized monkeys it appears that the concentration of sulfathiazole in the blood stream must reach at least 80 milligrams of the free drug with a total

concentration of 110 milligrams per cent before convulsions are produced. That these convulsions were not due to alkalosis was proved in the first animal by carbon dioxide combining power determination in the serum. When the blood level had reached its maximum, the carbon dioxide combining power was 65.4 volumes per cent. This problem warrants further investigations, for it may have considerable clinical significance.

Sulfadiazine next to sulfathiazole in its *in vivo* potency has been found to have little if any effect on the electrical activity of the cortex in monkeys. No excitatory activity or epileptiform spikes resulted from its use and clinical seizures have not been observed in the animals.

Sulfapyridine, the *in vivo* antibacterial activity of which is said to be 10 times less than sulfathiazole we feel is not epileptogenic or excitatory and, on the encephalographic evidence, would not hesitate to support its uses on the human cerebral cortex. Other factors, however, make it undesirable—its low solubility and the fact that its activity does not approach that of sulfadiazine and is estimated to be but 5 times the potency of sulfanilamide.

Sulfanilamide, aside from slight depression of the electrical activity, has no undesirable electrical side effects. It does not stimulate or cause epileptiform waves. Its solubility makes it a valuable adjunct to use in connection with sulfadiazine.

For contaminated and potentially infected and infected wounds of the brain, sulfapyridine may be discarded because it is not as efficient as antibacterial agent as sulfadiazine and less soluble than sulfathiazole. Sulfathiazole is epileptogenic and contraindicated. A combination of sulfanilamide and sulfadiazine for wounds of the brain would seem on the basis of experimental evidence, gained from this study and from the histological and bacteriological studies of others, to be the drugs of choice. Used in combination a high concentration of the more soluble sulfanilamide is obtained early and the more efficient, but the more insoluble sulfadiazine provides for prolonged action.

In these studies sulfonamides have been used singly and not in combination. We have used them in combination on the human brain. For the most part, combinations of sulfanilamide and sulfapyridine have been used but also sulfanilamide and sulfadiazine. In a few patients mixture of sulfanilamide, sulfapyridine and sulfathiazole have been applied directly to the brain without the subsequent production of epileptic

seizures. This raises the question of the possible suppression of the epileptogenic potency of sulfathiazole when used in combination with other sulfonamides. Experiments designed to test this hypothesis are now in progress.

Though it may seem to be out of place in this paper, it is important to point out again that these compounds act as foreign bodies in the brain, and they should always be used circumspectly and, of course, should be sterile.

#### SUMMARY AND CONCLUSIONS

The effect of microcrystalline preparations of sulfanilamide, sulfapyridine, sulfadiazine, and sulfathiazole applied to the surface of the uninjured cerebral cortex or injected into the injured brain of unanesthetized monkeys has been studied with electroencephalographic records taken from the surface of the dura or pia-arachnoid. The effect of the intravenous administration of the sodium salt of sulfathiazole upon the electrical activity of the cortex was also studied in unanesthetized monkeys.

1 Sulfathiazole applied directly to the cerebral cortex has a marked excitatory action causing local epileptiform discharge and convulsions which develop into severe generalized epileptic seizures.

2 Sodium sulfathiazole, injected into the blood stream, will produce epileptic convulsions only after the concentration of unconjugated drug has exceeded 80 milligrams per cent with a total concentration of over 110 milligrams per cent. Definite excitatory effects may be observed in the electroencephalogram with blood levels ranging between one-quarter and one-half these amounts.

3 Sulfanilamide, sulfapyridine, and sulfadiazine applied to the uninjured cortex cause no detectable change in its electrical activity nor any clinical evidence of altered function. Injected into the injured cortex these drugs cause a slight transient depression of electrical activity and a transient increase in the amount of slow wave activity following the injury, but no evidence of excitatory or epileptogenic action.

4 A combination of sulfanilamide and sulfadiazine is suggested as the preparation of choice for topical application to the brain on the basis of relative solubility, antibacterial action, and freedom from irritative action on cerebral tissue.

5 Sulfathiazole should not be used on the human brain.

#### REFERENCES

- 1 ADRIAN, E. D. Personal communication.
- 2 BOTTERELL, E. H., CARMICHAEL, E. A., and COLE, W. V. J. Neur. Psychopath., Lond., 1941, 7, 151, 154.
- 3 GREEN, H. N., and PARFITT, T. Lancet, Lond., 1942, 2, 205-210.
- 4 HURTEAU, EVERETT F. Canad. M. Ass. J., 1942, 46, 352-355.
- 5 Ibid., 1942, 46, 15-17.
- 6 INGRAM, FRANC D., and ALEXANDER, G. L. England J. M., 1942, 227, 374-375.
- 7 LYONS, CHAMP, and BURBANK, CHARLES. Surg., Gynec. & Obst. (Internat. Abstr. Surg.), 1942, 74, 11.
- 8 NAFFZIGER, H. C. Personal communication.
- 9 PILCHER, C., ANGELUCCI, R., and MEYER, W. J. Am. M. Ass., 1942, 119, 927.
- 10 RUSSELL, D. S., and FALCONER, M. A. Lancet, Lond., 1940, 2, 100-101.
- 11 SPINAS, QUESLEY W., and JERNIST, J. J. Exp. Biol., N. Y., 1941, 47, 393-397.
- 12 TOFFEL, MAX, and GERMAN, W. J. Surgery, 1941, 1, 201.
- 13 Idem. Yale J. Biol., 1941, 14, 137-142.
- 14 WATT, A. C., and ALEXANDER, G. L. Lancet, Lond., 1942, 1, 493-496.

# TANNIC ACID AND LIVER NECROSIS

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Richmond, Virginia

WELLS Humphrey, and Coll have reported recently that subcutaneous administration of tannic acid results in liver necrosis in rats. They suggest that it does not seem improbable that the liver necrosis noted in many cases of severe burns may have been due to the toxic action of the tannic acid used in treatment rather than to the products arising from the burned tissue. Because of the widespread use of tannic acid in the treatment of burns, it was our opinion that confirmation of this work would be justified at this time. In addition, since the liver damage resulting from tannic acid administration is central and somewhat similar to that given by carbon tetrachloride, it was decided to study the possible protective action of sulfanilamide on tannic acid liver necrosis. Previous investigations by Forbes and associates (3) and others (4) show that oral administration of sulfanilamide increases the resistance of rats to both acute and chronic carbon tetrachloride poisoning. This protective action of sulfanilamide on the liver has also been found in acute chloroform poisoning in rats (5).

## EXPERIMENTAL

**Series 1.** Thirty milligrams of sulfanilamide per 100 grams of body weight was given by stomach tube to 4 rats late in the afternoon. This was followed immediately by the subcutaneous injection of 50 milligrams of tannic acid (U.S.P. granular) per 100 grams of body weight. The needle was always inserted about the middle of the back and the injection made just back of the neck. Similar amounts of tannic acid were given to 4 control animals. The sulfanilamide and tannic acid administrations were repeated next morning and on two additional mornings thereafter. The animals were sacrificed 24 hours after the last injection, and histological examination of the livers were made. All livers showed definite areas of necrosis and no apparent difference could be seen between those of the control and treated animals.

**Series 2.** Thirty milligrams of sulfanilamide per 100 grams of body weight was given by stomach

tube to 4 rats about 9:00 a.m. This was followed immediately by the subcutaneous injection of 1 cubic centimeter of a 10 per cent solution of tannic acid per 100 grams of body weight. Four control animals were given a corresponding amount of tannic acid. The sulfanilamide and tannic acid administrations were repeated next morning. All of the animals were sacrificed 24 hours after the last injection and their livers were examined histologically. Although there was no marked difference between the livers of the two sets of animals, those given sulfanilamide in addition were, if anything, slightly worse than those from the controls.

**Series 3.** Thirty milligrams of sulfanilamide per 100 grams of body weight was given by stomach tube to 4 animals about 9:00 a.m. Next morning another similar dose of sulfanilamide was given to the same rats. This was followed immediately by the subcutaneous injection of 1 cubic centimeter of 10 per cent tannic acid per 100 grams of body weight to these animals and to 4 untreated control animals. All were sacrificed 48 hours after this injection. On histological examination of the livers, those from the animals receiving sulfanilamide in addition to the tannic acid were slightly worse than those of the controls.

**Series 4.** Thirty milligrams of sulfanilamide per 100 grams of body weight was given to 3 animals by stomach tube. This was followed immediately by the subcutaneous injection of 1 cubic centimeter of 15 per cent solution of tannic acid per 100 grams of body weight. Similar amounts of tannic acid were injected into 1 control animal. Five of the rats receiving sulfanilamide and 3 of the controls were dead 8 hours later. Another control was found dead 24 hours later. All the remaining animals were sacrificed 48 hours after the tannic acid injections and their livers examined histologically. The livers of the sulfanilamide treated animals which survived were on the whole somewhat better than those of the surviving controls. However, in view of the fact that 50 per cent of the treated animals and only 30 per cent of controls died, it appears that the differences noted histologically were incidental rather than the result of sulfanilamide administration.

**Series 5.** Although the oral administration of sulfanilamide exerted no protective action against

From the Department of Biochemistry and Surgery, Medical College of Virginia. This study was conducted under grant from the Committee on Medical Research, Office of Scientific Research and Development.

the hepatotoxic action of tannic acid, it does not necessarily follow that similar results would be obtained if the two were injected subcutaneously in a single solution. Consequently, 1 cubic centimeter per 100 grams of body weight of a 12.5 per cent solution of tannic acid containing 30 milligrams of sulfanilamide, partly in solution and partly in suspension, per cubic centimeter, was injected subcutaneously into 5 rats. A similar amount of tannic acid without sulfanilamide was injected into 5 control animals. The animals were killed 48 hours after injection and their livers were examined histologically. Although there were no marked differences between them, the livers of the animals receiving sulfanilamide with the tannic acid were slightly worse than those of the control animals.

**Series 6** Since subcutaneous xanthine injection is known to increase a rat's resistance to the hepatotoxic action of carbon tetrachloride (5), it was decided to determine if it would have a similar action against tannic acid. One hundred milligrams of a xanthine suspension in water per 100 grams of body weight were injected subcutaneously just back of the tail, into 4 rats. Forty-eight hours after they, along with an equal number of controls, were given an injection of 1 cubic centimeter, of a 12.5 per cent tannic acid solution per 100 grams of body weight. All the animals were sacrificed 48 hours later, and their livers were histologically examined. No evidence of any protective action from the xanthine injections was obtained.

#### OBSERVATIONS

Tannic acid administration to the rat appears to give a fairly uniform and rather specific liver lesion. In most of the sections studied in these experiments the necrosis of the liver was almost always central with the remainder of the liver lobule, especially the periphery, remaining almost normal. We have not seen in our sections the numerous mitotic figures described by Wells but there has been infiltration of the interstitial tissue with leucocytes. Figure 1 illustrates a typical section of liver of a rat which has received 1 cubic centimeter of a 12½ per cent solution of tannic acid per 100 grams of body weight. It is representative of most of the sections obtained in this study.

It is disappointing that we found no protective action of any of the substances studied against the hepatotoxic action of tannic acid. Substances which give fairly good protection against carbon tetrachloride and chloroform, such as sulfanila-

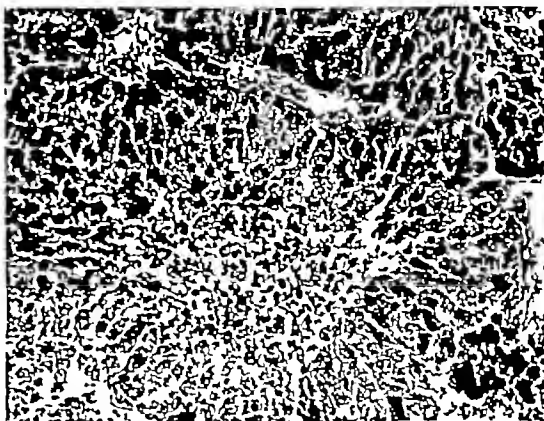


Fig 1 Typical section of the liver of a rat given 1 cubic centimeter of a 12½ per cent solution of tannic acid per 100 grams of body weight

uide and xanthine, afford practically no protection against tannic acid. For this reason we are inclined to the view that the mechanism of action of tannic acid may be quite different from that of chloroform and carbon tetrachloride. In a search for substances that might possibly protect the liver against tannic acid poisoning, the studies herein reported indicate that investigations should not be limited to those substances that protect the liver against carbon tetrachloride and chloroform poisoning. In other words, it is more than likely that high carbohydrate and high protein diets will afford no protection to the liver of a burn patient who has been treated with tannic acid.

#### SUMMARY

The hepatotoxic action of subcutaneous tannic acid injections has been confirmed. No protective action was given, either by the oral or subcutaneous administration of sulfanilamide or the subcutaneous administration of xanthine.

#### REFERENCES

- 1 FORBES, J. C., and EVANS, E. Unpublished results
- 2 FORBES, J. C., LEACH, B. E., and WILLIAMS, G. ZUR Protective action of sulfanilamide against liver cirrhosis from chronic poisoning with carbon tetrachloride. In press
- 3 LEACH, B. E., and FORBES, J. C. Proc Soc Exp Biol, N. Y., 1941, 48: 363
- 4 MACHELLA, T. E., and HIGGINS, G. M. Am J M Sc, 1942, 204: 194
- 5 NEALE, R. C., and WINTER, H. C. J Pharm Exp Ther, 1938, 62: 127
- 6 WELLS, D. B., HUMPHREY, H. D., and COLL, J. J. N. England J M., 1942, 226: 629

# INJURIES TO THE LARYNX AND TRACHEA

ROBERT L. NACH, M.D. and MILTON ROTHMAN, M.D. New York, New York

**I**NJURY to the larynx and trachea, though not uncommon, is infrequently reported in the literature. Since these cases are ordinarily handled at the outset by the general surgeon, the material is offered from such a perspective. The following is based on a study of 7 cases of injury to the laryngotracheal passage treated by the surgical service of the Harlem Hospital the past 6 years. Fourteen of these were serious direct wounds of the larynx or trachea whereas 3 were of the subcutaneous rupture type.

The greater number of reports that have appeared in the literature have dealt principally with the subcutaneous rupture type. Isolated instances of cut throat or laceration of the trachea or larynx have been described. Scott described what he believed to be the first reported case of complete division of the trachea and esophagus, the result of accidental injury. In this instance the divided esophagus, trachea and soft parts were successfully united by primary suture. Bailey reports his experience with 57 cases of cut throat. Zeech in presenting a case of subcutaneous rupture of the trachea tabulated the results of 53 similar cases found in the literature up to that time.

## ETIOLOGY

**A Lacerations.** Although suicidal attempts are by far the most frequent cause, there are various other mechanisms, some of which may be quite bizarre. In the majority of lacerations of the neck requiring surgical aid, vital structures remain involved, the trauma being confined to the skin, platysma or neck muscles. The mobility and redundancy of the trachea and larynx undoubtedly preclude greater frequency of injury to these parts. The limited protection afforded by the chin, sternum, and lateral neck musculature tends to restrict the incidence of injury.

**B Subcutaneous rupture.** Subcutaneous injury to the upper air passages, though usually the result of direct trauma, may be due to indirect violence. Sunderland reported the case of a boy who in fright suddenly threw his head backward with resultant subcutaneous rupture of the trachea. Andre described a similar injury in a 19 year old

primipara occurring during the course of a severe labor. Latour, Brotschneider and Gerstel each described instances of subcutaneous rupture resulting from severe coughing spells. In Lebert's case the injury followed equal efforts to remove a foreign body from the trachea. Nixon reported a most unusual case of spontaneous rupture of the trachea with no describable cause. The onset was that of a spontaneous, rapid, crepitating swelling which simulated a large goiter and which became larger with expiration and smaller with inspiration. Shortly afterward spontaneous rupture of the air occurred posterior to the right angle of the jaw with 2 other ruptures in the vicinity of the right axilla. Exploration of the neck showed the rupture to have been in the thoracic portion of the trachea. A low tracheotomy was followed by an uneventful recovery.

One explanation for such occurrences is the mobility of the neck, which is surmounted by a top-heavy pendulous head. Zeech believes that an important predisposing factor is the increase of intratracheal pressure due to holding of the breath, and that this is produced by closure of the epiglottis, a physiological reflex occurring at times of physical stress. Under such circumstances it is conceivable how direct or indirect trauma may produce a rupture of this hollow inflated sac, a situation analogous to the comparative ease of traumatic rupture of a distended urinary bladder. Desjardins and associates describe a case of a comminuted fracture of the trachea in a 70 year old male, the result of a home kick which was successfully treated by emergency tracheotomy. Because of the lateral mobility of the trachea it is obvious that a damaging blow ordinarily must be directed in an anteroposterior direction so as to compress the part against the rigid spinal column.

## PATHOLOGY

The pathological condition will vary with the nature and degree of the trauma. The lacerations or rents will be either transverse, oblique or vertical, the transverse type being the most common. When the striking agent has a sharp edge such as a razor or a piece of glass, the tracheal or laryngeal wound is likely to be a cleanly divided one. More crude instruments of trauma and crushing injuries will produce rents or fractures. The lateral annular membrane alone may be divided, the car-

From the Surgical Service of the Harlem Hospital, Dr. Clarence Hawley, Director.

Presented before the Surgical Section, New York Academy of Medicine, December, 1942.

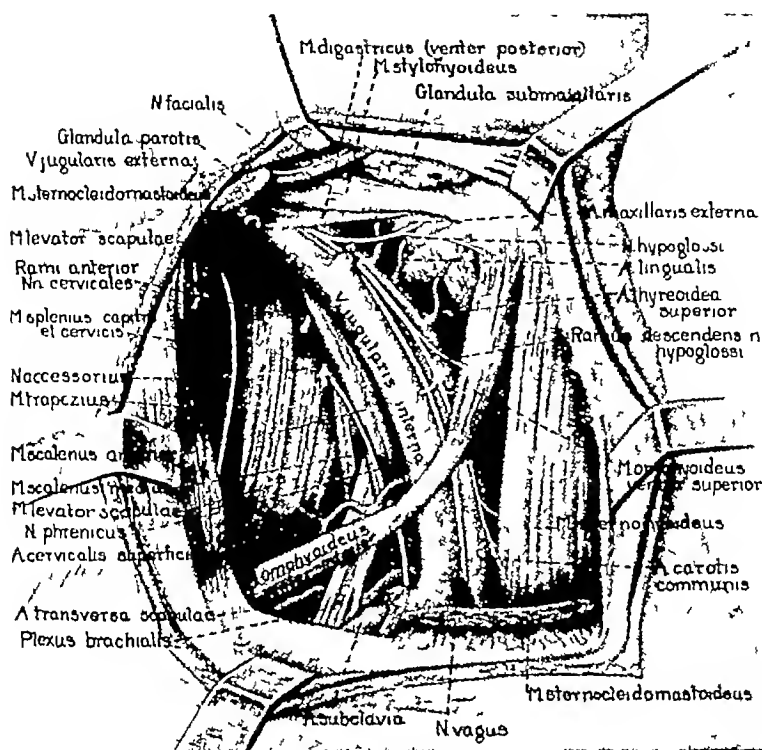


Fig 1 In the lower portion of the neck the great vessels are much closer to the surface so that at the same depth a laceration, which higher up would not be serious, would be apt to injure one or more of these vessels (From Callander's *Surgical Anatomy*, 2d ed, 1939 Saunders)

laminous portions of the tracheal rings remaining intact. Perforations may result from gunshot injuries or puncture wounds. Tracheal fractures are apt to be irregular and occasionally are comminuted. Subcutaneous rupture can result without evidence of injury to the skin or soft parts, and may occur as low as at the bifurcation of the trachea. Varying portions of the trachea or larynx may be torn away by shot, shell, or other severe forms of trauma.

Bailey divides injuries to the laryngotracheal tract into 5 groups according to the anatomical location of the trauma, namely (1) wounds above the hyoid bone, (2) wounds of the thyrohyoid membrane, (3) wounds of the thyroid cartilage, (4) wounds above, below or through the cricoid cartilage, and (5) wounds of the trachea.

Associated injuries to the esophagus, pharynx, blood vessels, or contents of the carotid sheath are as likely to occur as not. Death may follow promptly before adequate surgical treatment can be rendered. Bleeding may be severe, and in the

case of subcutaneous rupture reported by Taylor, death was due to drowning by blood which filled the lower end of the trachea, the bronchi, and the bronchioles. Following complete division of the trachea, retraction of the ends usually follows and the lower part may disappear behind the sternum. With a severe contusion, submucosal hemorrhage, occasionally severe enough to occlude the lumen of the trachea, might result. Post-traumatic edema of varying degree may ensue with partial or complete obstruction to the airway.

The likelihood of injury to the contents of the carotid sheath will depend upon the level of the trauma. In the upper part of the neck, the great vessels are deeply situated and frequently escape injury. In the lower portion they are much closer to the surface so that the same depth of a laceration which higher up might not be as serious would, at this level, injure one or more of the great vessels of the neck. Hemorrhage from such associated large vessel trauma frequently will be fatal before surgical aid can be offered.



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**I**NJURY to the larynx and trachea, though not uncommon is infrequently reported in the literature. Since these cases are ordinarily handled at the outset by the general surgeon, the material is offered from such a perspective. The following is based on a study of 17 cases of injury to the laryngotracheal passage treated by the surgical service of the Harlem Hospital in the past 10 years. Fourteen of these were various direct wounds of the larynx or trachea, whereas 3 were of the subcutaneous rupture type.

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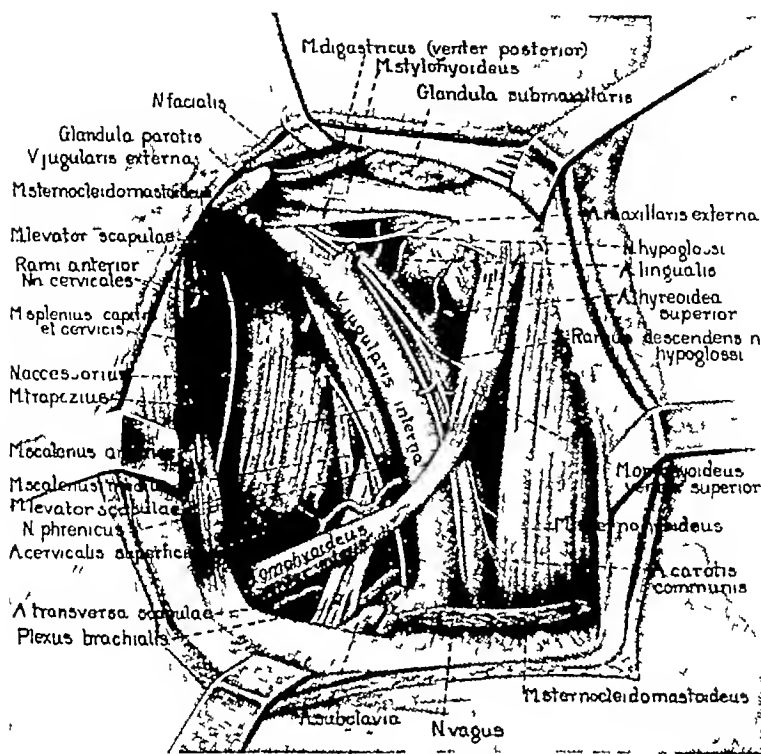


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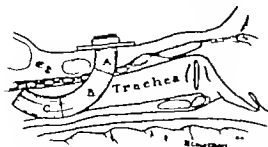


Fig. 1. Composite view of tracheal cannulae: too short, *b*, proper length, too long, as it permits end of cannula to impinge against wall of trachea.

### SYMPTOMS

When the tracheal or laryngeal wound communicates with the skin surface the nature of the injury and the respiratory rush of air and bloody froth through the wound make the situation quite apparent. Dyspnea, cyanosis, and cough will be present in varying degrees.

The subcutaneous rupture type is usually characterized by the prompt appearance of symptoms the most common of which is a rapidly spreading subcutaneous emphysema. The latter is often out of proportion to the degree of injury. The earliest clinical manifestation of a rupture of the intra-thoracic trachea is likely to be a subcutaneous

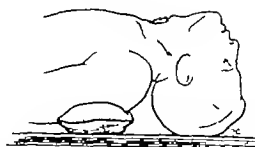


Fig. 2. Proper position for surgical procedures on the trachea. The mouth and folded sheet is placed underneath the shoulders and not behind the neck. The head is fairly extended so that the larynx and sternal notch are in the same straight line.

emphysema appearing in the suprasternal notch (15). Occasionally there may be an appreciable interval before the onset of symptoms. In the case described by Jackson and Jackson, in which a subcutaneous injury to the trachea did not make itself clinically evident until several hours had elapsed. The subcutaneous emphysema may appear and extend with such rapidity as to involve the entire body including the eyelids and scrotum within a hour or two. With the subcutaneous type of injury particularly if there is tearing of the tracheal mucosa, localized pain, dyspnea, cough, cyanosis, wheezing and a bloody mucoid expectoration are the chief signs. Should the lesions be at the level of the larynx, inspiratory retraction of the suprasternal notch, characteristic of laryngeal obstruction, will become manifest. Palpation of the neck occasionally may disclose an alteration in the normal contour of the larynx or trachea or even separation of the divided tracheal ends. Ecchymosis, edema, or hemorrhagic infiltration of the soft tissues of the neck may be variable features. Hoarseness or aphonia commonly accompany laryngeal trauma because of the associated submucosal hemorrhage and edema.

The danger in the use of morphine under such circumstances must be emphasized. Its administration, by alleviating respiratory distress and dyspnea may be responsible for failure of or a sorry delay in diagnosis. Unrecognized aphonia due to edema of the trachea or hemorrhage or submucosal hematoma may result from such narcosis.

### DIAGNOSIS

When a gaping wound is present, the diagnosis is self-evident. With the subcutaneous type of injury a history of direct or indirect trauma in conjunction with the group of symptoms previously described, namely subcutaneous emphysema, cough, dyspnea, respiratory distress and bloody



Fig. 3. A cannula that can be improvised from a piece of hard rubber tubing, should the need arise.



Serious bleeding which is frequently present, must be controlled. The divided air passages may be dealt with in a number of ways, governed by the nature of the injury and the attendant symptomatology. The procedures that may be used in dealing with the severed air passage are (1) primary suture without complementary tracheotomy (2) primary suture with complementary tracheotomy (3) introduction of a cannula into the tracheal wound and (4) anchoring the distal end of a completely divided trachea into the wound.

Primary suture without complementary tracheotomy is indicated when the air passage has been lacerated by a sharp instrument, as in the ordinary case of cut throat. This procedure had been followed in 7 cases in our series without any subsequent complications. When there is respiratory distress with primary suture, or when such distress is anticipated because of associated edema, hemorrhage or tissue trauma, complementary tracheotomy is indicated. Instead of performing a complementary tracheotomy the operator may elect to introduce a tracheotomy tube into the wound in the air passage, with or without partial suture of such wound. Such a procedure would be governed by the nature of the wound and the urgency with which it must be completed. Occasionally when there is complete division of the trachea, re-establishment of continuity may not be possible because of irreducible retraction of the divided ends. In such an instance as a life-saving procedure it will become necessary to anchor the distal end into the wound, preferably with a tracheotomy cannula in place. This was done in one of our cases, with recovery from the acute episode and subsequent discharge from the hospital. As is rarely the case, the distal end may retract behind the sternum, leading extreme difficulty to primary repair or to the introduction of a tracheotomy tube. In such a situation an improvised rubber tube cannula can be introduced and more satisfactorily retained in the distal end of the trachea.

**C. Intermediate wounds.** It is in the intermediate type—the wound in which it is evident that injury of the trachea or larynx is not too big and the patient presents no respiratory distress, no increasing subcutaneous emphysema and but little bleeding—that the decision for or against surgical intervention always cannot be readily made. The potential danger of sudden acute asphyxiation must be borne in mind even when the situation appears to be under control. Richards, quoted by Remy Nérès, reported an instance of sudden fatal asphyxiation in a patient suffering from a symp-

tomatic bullet wound of the trachea. The advantage to both the patient and the surgeon of a tracheotomy performed without haste is self-evident. An attempt to execute the procedure under the duress of asphyxiation, a rapidly developing subcutaneous emphysema, or a pulmonary complication, may be very trying. The necessity for prophylactic tracheotomy should be seriously considered in instances in which respiratory obstruction may be anticipated, or in which careful and adequate observation cannot be rendered.

If the pharynx has been entered, as may be the case with wounds above the hyoid bone or through the thyrohyoid membrane the edges of the pharyngeal mucous membrane should be carefully trimmed and reunited with interrupted chromic catgut sutures. A severely injured submaxillary gland can be removed.

**Epi-glottis.** With wounds through the thyrohyoid membrane or above the hyoid bone the epiglottis may be partially or completely divided. Repair of the epiglottis should be attempted using absorbable sutures. Sutures ordinarily hold well in this location. Bailey reports an instance in which a fragment of over an inch was removed without effect. Successful repair of partial laceration of the epiglottis was done in one of our cases.

**Lacerations of the esophagus.** Lacerations of the esophagus must be carefully repaired, an adequate anastomosis being suggested in the literature. The technique of esophageal suture as described by Scott is a good one. In his case of complete division of the esophagus and trachea, satisfactory suture repair was made. In treating the esophagus, interrupted chromic catgut sutures are used, the posterior mucous coat being approximated first, and the posterior mucous membranous next, the knots being tied on the inside of the lumen. The anterior mucous membrane is then sutured, the knots being tied external to the lumen. Finally the anterior muscular coat is sutured. This method was employed in the case of complete tracheo-esophageal laceration in our series. When found to be divided, the deep fascial and constrictor muscles should be reunited.

**Gastrostomy.** With associated injuries to the pharynx or esophagus, gastrostomy may become necessary in order to safeguard the suture line, to minimize the possibility of infection, and to insure adequate nutrition. Such procedure may be done directly following the wound repair, or at any time during the postoperative course, should the indication arise. In the case in our series, it was performed on the 31st postoperative day because of feeding difficulties. As an alternative, feeding tube may be passed through the nasopharynx into the stomach at the time of operation.

**Sutures of the trachea and thyrohyoid cartilage.** Lacerations of the thyroid cartilage and trachea are to be sutured whenever feasible. Cartilage, particularly the thyroid cartilage is notoriously difficult to repair as the suture tends to cut through. Approximation can be successfully effected if the needle used is not too big, and if one uses mattress sutures which are not tied too tightly. The trachea lends less difficulty since the suture can be passed around the tracheal rings above and below the laceration. These sutures, preferably of fine chromic catgut, should be interrupted, and wherever possible should be tied on the outside. With complete division of the trachea, it is obvious that the sutures suturing the posterior wall must be tied on the inside of the lumen. Careful approximation is required.

avoid complicating subcutaneous emphysema or local infection. With separation of the tracheal ends following complete division or rupture, approximation and suture may be performed if this separation does not exceed 2 to 4 centimeters. Beyond this limit of separation the suture line is apt to give way (Gluck, Nowakowsky). If the strength of the suture line is in doubt, the latter can be reinforced by a pedicle muscle flap taken from the sternomastoid or ribbon muscles. Such reinforcement will help protect the overlying tissues against complicating infection or subcutaneous emphysema.

*Repair of defects with fascial transplants.* Relative to the repair of laryngotracheal defects, the experimental work of Taffel is suggestively promising in its clinical application. This worker was able to effect an airtight repair of resected full-thickness segments of the trachea and bronchus in dogs by means of free fascial grafts. Such fascial grafts provided immediate restoration of the airway, thus preventing any leakage of air or secretions. As in other sites these fascial transplants undergo connective tissue replacement, the latter remaining as a permanent supporting structure firmly covering the defect. As described by Taffel, "the new and final structures which served to restore the continuity of the viscus were composed of (1) an inner layer of pseudostratified epithelium, (2) a layer of submucosa with occasional mucous glands and a few small islands of new cartilage, but with occasional exceptions, no fibers of muscularis mucosa, and (3) an outer layer of supporting adult connective tissue." This procedure possesses potential clinical application in instances in which loss of a considerable amount of substance from the laryngotracheal tract has occurred. Fascia in amount adequate for such purpose is readily obtainable from the region of the neck wound as well as from the customary source in the thigh.

*Use of the sulfonamides.* Because of their proved value in traumatic wounds, and because of the seriousness of suppuration in the deep layers of the neck, these potentially infected wounds involving the air passages and esophagus should be treated by the routine implantation of the sulfonamides into the adjacent tissues. Supplementary oral or parenteral administration of these drugs may be necessary.

*Tracheotomy.* It must be emphasized that tracheotomy, when indicated, should be done early and not hurriedly. When delayed and hastily performed, the procedure may be trying to the surgeon and dangerous to the patient. The distinction between high and low tracheotomy in relation to the thyroid isthmus is no longer of great importance since surgeons have learned how to divide this structure quickly and safely. The method of dividing the thyroid isthmus as described by

Digby is most helpful. Controversy between the use of laryngotomy and tracheotomy still exists. The English surgeons have commonly practiced laryngotomy for wounds above the level of the cricoid cartilage, inserting the laryngotomy tube through the cricothyroid membrane. Laryngologists in this country, particularly Chevalier Jackson, have decried high tracheotomy because of the frequency of ultimate perichondritis and laryngeal stenosis. In our series all tracheotomies performed were of the low type. There were no immediate tracheotomy complications. Because of the difficulty of follow-up in these patients, it is impossible to state whether there were any delayed sequelae.

*Anesthesia.* Local anesthesia is by far the safest. Under such conditions, general anesthesia is dangerous, it abolishes the action of the accessory muscles of respiration, the function of which is so important in the presence of obstructive dyspnea. If a general anesthesia is required, as in the case of a child, it is most safely administered through a bronchoscope.

*Position of the patient.* This is an important detail. The patient is restrained on the table in the appropriate manner. A sandbag or rolled up sheet is placed underneath the patient's shoulders—not underneath the neck. The head is then fully extended so that the chin and sternal notch are in the same straight line (Fig. 3). An assistant placed to the left of the patient's head is designated to immobilize the head in this position by placing the right hand over the frontoparietal region and the left hand under the occiput.

*Technique of tracheotomy.* An adequate midline incision is made from the thyroid notch to the suprasternal notch. The cricoid is identified and the dissection is continued in depth below this point. The prethyroid muscles are separated in the midline, thus exposing the trachea and thyroid isthmus. The isthmus can be retracted upward if not too large, but if it overlies the site of the tracheotomy, it is safer to divide it. Avoidable mortalities have occurred because of the slipping of a large undivided thyroid isthmus back over the tracheotomy opening during the early post-operative period when the cannula has either been removed for cleansing purposes or has slipped out. Division of the thyroid isthmus is best accomplished in the manner described by Digby. A transverse incision is made in the fascia at the lower border of the cricoid, thus exposing the trachea above the thyroid isthmus. A curved hemostat passed posterior to the isthmus from above downward bluntly separates the latter from the trachea, the hemostat being opened and closed to

facilitate its passage. The isthmus which is clamped by two parallel placed hemostats is then divided. The isthmus is freed further from the trachea by externally rotating the hemostats, at the same time slightly depressing the handles so as to elevate the points. Supplementary sharp dissection may be necessary. Conditions permitting, all hemostats should be effected before the trachea is opened. The cricoid is steadied by means of a sharp hook which is pulled in an upward direction. The trachea is opened by a vertical midline incision through the 3rd, 4th, and 5th rings. The knife is held in the manner of a pen with the sharp edge directed anteriorly, so as to avoid laceration of the posterior wall of the trachea. The tracheal opening is gently separated with a Trouseau dilator or a hemostat and a cannula is inserted. Instead one can make an oval window in the trachea just large enough to admit a cannula.

For a "tranquil tracheotomy" Thompson advises the intratracheal instillation of 20 drops of 1 per cent cocaine through a hypodermic syringe. The liquid thus introduced into the trachea may cause a slight cough but no distress. After 10 minutes, if conditions permit, the trachea can be opened and the tracheotomy tube introduced without any cough or spasm.

In the choice of a tracheotomy cannula, adequate length is important. Too short a cannula may slip out of or be pulled from the trachea by careless handling or by postoperative soft tissue swelling with resultant asphyxia.

The skin about the tracheotomy cannula should not be sutured too closely. This might cause a retention pocket for the tracheobronchial secretions which pass out alongside of the tube with the danger of complicating local infection.

**Emergency tracheotomy** When asphyxiation is acute, promptness and speed of action may be life-saving measures. The details of technique just described may of necessity be waived aside. If cyanosis is marked and breathing has ceased, one may not countenance any delay, not even for local anesthesia. The procedure should be rapidly executed, but with care and precision. The head is fully extended as described. The operator standing to the patient's right, places the thumb and middle finger of his left hand on either side of the trachea, making sustained pressure posteriorly and laterally against the sternomastoid muscles and the underlying carotid sheaths. This throws the trachea into prominence. An adequate midline incision is made from the thyroid notch to the suprasternal notch. Suction when available, will help to keep the operative field free of blood.

With the thumb and middle finger in position, the left index finger is passed along the left side of the trachea. The scalpel is placed medial to the index finger so that the 3rd, 4th, and 5th tracheal rings are incised in the midline. Despite the haste and free bleeding care should be exercised to avoid cutting the cricoid or thyroid cartilages or the posterior wall of the trachea. The tracheal wound, held open by a Trouseau dilator or hemostat, is then cannulated. The head is lowered and turned to one side so as to permit the blood to run away from the tracheal wound. If breathing has ceased, artificial respiration should be given and oxygen passed through the cannula, but not too forcibly. Hemostasis is then effected. When the ordinary tracheal cannula is not available, or should it be too short, one can be improvised from a piece of firm rubber tubing, reaching if necessary to the bifurcation of the trachea.

**Complications** The literature appears to be indefinite concerning the immediate complications. Jackson and Jackson state that bronchopneumonia is infrequent, whereas Bailey cites the frequency of this complication. In our series there were no immediate pulmonary sequelae. Four of the patients developed wound infections which were readily controlled by local treatment. Since these patients have been treated on an acute traumatic surgical service, we are not in a position to report on the delayed complications such as stricture or perichondritis. Moreover any such complications would come to the attention of the laryngologist. Remy-Néris mentions the apparently greater incidence of pulmonary tuberculosis following injury to the laryngotracheal tract. We are in no position to comment upon this inference.

#### ANALYSIS OF CASES

In our series there were 17 cases of injury to the larynx and trachea. Three of these were subcutaneous ruptures of the trachea. Of the remainder 13 were the result of lacerations and one was caused by a gunshot. All patients were admitted to the hospital within 3 hours following injury. The mortality rate was 5.8 per cent for the entire series. The one patient who died was admitted in shock with an associated laceration of both external jugular veins. Shock was never relieved and death occurred on the operating room table.

In 7 cases, immediate primary repair of the tracheal wound was performed without complementary tracheotomy. One patient had a tracheotomy tube inserted into the original wound. Because of further bleeding and dyspnea in this case the tracheal wound was repaired within 4 hours

## ANALYSIS OF CASES

Initial Color Sex	Weapon	Injury	Associated injury	Procedure	Course	Stay in hospital
1 N T C M	Knife	Thyroid cartilage	Laceration of submaxillary gland	Immediate repair	Uneventful	Signed out 2 days
2 N S C M	Knife	Thyroid cartilage	Shock multiple lacerations	Immediate repair	Uneventful	13 days
3 H W C M	Knife	Thyrocricoid membrane	Stab wound of chest with pneumothorax shock	Tracheotomy tube into original wound, primary repair	Uneventful	18 days
4 F M C M	Knife	Thyroid cartilage	Shock	Immediate repair	Infected	17 days
5 P T C M	Knife	Trachea		Immediate repair	Uneventful	8 days
6 J Q W M	Knife	Thyrohyoid membrane Pharynx exposed Partial division of epiglottis	Shock, lacerations of chest and wrist	Repair of laceration and epiglottis, low tracheotomy	Uneventful	12 days
7 C N C M	Gunshot	Trachea	Anterior jugulars	Immediate repair	Infected	24 days
8 C W C M	Knife	Complete division through thyrocricoid membrane	Complete division of esophagus	Esophagus reconstructed. Posterior trachea closed. Tracheotomy tube into anterior opening	Gastrostomy on 13th day	46 days
9 S M C M	Knife	Trachea	Multiple lacerations	Unable to close trachea Packed	Uneventful	12 days
10 A M C M	Knife	Trachea		Immediate repair	Uneventful	11 days
11 W H C M	Knife	Trachea		Tracheotomy into original wound because of bleeding, reoperated upon in 4 hrs. and trachea repaired. No tracheotomy	Uneventful	14 days
12 L P C M	Knife	Trachea	External jugulars, shock	Immediate repair	Died of shock on table—4 hrs	
13 L H W M	Knife	Trachea	Amputation of penis	Immediate repair of trachea	Uneventful	14 days
14 N G W M	Knife	Trachea	Penetrating stab wound of chest with pneumothorax	Tracheotomy into original wound	Uneventful	15 days
15 H M C F	Auto accident	Subcutaneous rupture of trachea		Conservative until tracheotomy on 4th day	Infected	Signed out 13 days
16 I M C F	Kicked	Subcutaneous rupture of trachea	Incision of soft parts to relieve subcutaneous emphysema no repair		Infected	17 days
17 W B C M	Kicked	Subcutaneous rupture of trachea		Conservative	Uneventful	6 days

without complementary tracheotomy. In another instance, the divided tracheal ends were too far apart to permit accurate approximation. The intratracheal tissues were packed without tracheotomy. One patient had the original wound closed and a low tracheotomy tube inserted. In the patient with the combined esophagus and trachea injury, after reconstruction of the esophagus and posterior trachea, a tracheotomy cannula was in-

serted into the anterior portion of the tracheal opening. This patient also required a gastrostomy on the 13th day. In 1 case the laceration extended through the thyrohyoid membrane into the pharynx with partial division of the epiglottis. In 5 patients a tracheotomy tube was inserted into the original traumatic opening.

Of the 3 cases of subcutaneous rupture, one patient was treated conservatively. Another was



treated conservatively until marked dyspnea resulted on the 4th day when an emergency tracheotomy was performed. In the third case small puncture wounds were made in the skin of the neck to relieve the subcutaneous emphysema.

All operative procedures were carried out under local anesthesia except in one case in which intravenous evipal was used. Five patients were admitted in shock, one of whom never recovered. Two patients developed a tension pneumothorax from associated stab wounds of the chest. There were no other pulmonary complications. Complicating wound infection occurred in four instances. The average stay in the hospital for all types of cases was 28 days.

#### SUMMARY

1. The results of a study of trauma to the laryngotracheal tract are offered from the perspective of the general surgeon rather than that of the laryngologist. Consideration has been given to instances of subcutaneous rupture as well as those due to direct trauma.

2. Successful results, particularly with the subcutaneous rupture type, are contingent upon early recognition and the institution of appropriate treatment.

3. The necessity for the maintenance of an adequate airway either by operative repair tracheotomy or bronchoscopy has been stressed.

4. The potential danger of asphyxia by the careless use of sedatives has been emphasized.

5. The appropriate types of treatment have been considered.

6. The technique for the elective and the emergency types of tracheotomy has been described in detail.

7. The various complications have been considered.

8. The mortality rate in our series was 1 case in 17 or 5.8 per cent. This 1 death appears to have been due to hemorrhage and shock rather than the injury to the trachea *per se*. The remainder of the patients were successfully handled by various forms of treatment rendered in accordance with the nature of the injury and the presenting symptoms.

#### BIBLIOGRAPHY

1. BAILEY, H. *Surgical Emphysema*. 4th ed. pp. 540-542. Baltimore: Williams & Wilkins Co. 1929.
2. BARNES, G. E. *Surgery of the Larynx and Trachea*. Keen Surgery Vol. III, pp. 260-72.
3. DRAJACOVIC, BOWETT, and MORTIMER KIRBY. *Lyon* 1910, 163, 700-7.
4. DUBOIS, K. H. *Lancet*, Lond., 1905, 34.
5. GILLBERT, A. J. *Pennsylvania M. J.* 1910, 11, 67-68.
6. JACKSON, C. and JACKSON, C. L. *Surgery of the Larynx and Trachea*. Lewis' Fracture of Surgery Vol. IV, Chap. 7.
7. PARSONAGEAS, R. C. *Radiology*, 1914, 16, 404-406.
8. REED, NICHOL, G. J. *Med. Tr.* 1894, 10, 30-34.
9. RICHMOND, A. P. and GOLDBERG, A. S. *Texas J. M.* 1917, 68, 1605-1606.
10. SCOTT, G. D. *J. Am. M. Ass.* 1912, 90, 649-650.
11. STEIN, A. J. *Texas J. M.* 1913, 13, 6, 5-10.
12. TAPPIN, M. *Surgery* 1900, 8, 38-7.
13. TAYLOR, J. J. *Lancet*, Lond., 1914, 99, 301.
14. THOMPSON, SIR ST. CLAIR. *Diagnosis of the New and Throat*, 4th ed. pp. 804-809. London, 1917.
15. WRIGHT, L. T. Personal communication to the writers.
16. ZATSEV, L. H. *Illnesses M. J.* 1912, June, p. 43.

# EXPERIMENTAL HEAD INJURY WITH SPECIAL REFERENCE TO THE MECHANICAL FACTORS IN ACUTE TRAUMA

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**T**HIS view has been presented that the effects of cranial trauma are more profound to the nonfixed than to the fixed head. Experimental data have been submitted to show that injury of a critical velocity suddenly setting the head into motion may produce unconsciousness (concussion) and even death (6). Under these circumstances, pathological changes in the brain were absent or, if present, were considered to be incidental.

In our experience, the physiological effects observed in patients with head injury have seemed, in general, to correlate with the intensity of the injuring force and the pathological changes produced in the brain. In order more clearly to understand the mechanics of injury as related to the physiological and pathological effects, experiments were performed upon 150 dogs by varying the type and intensity of the injury to the fixed and nonfixed head.

## METHOD AND PROCEDURE

Mongrel dogs with an average weight of  $8.51 \pm 2.87$  kilograms were used for the study. Morphine in quantities of 20 milligrams per kilogram was the anesthetic used in the experiments. Before injury, the scalp and masseter muscle were infiltrated with 1 per cent procaine solution and then reflected from the bone. The striking objects made direct contact with the parieto-occipital bone. The blood pressure was recorded from the femoral artery, respirations, by means of a balloon about the thorax. The spinal fluid pressure was recorded from a needle inserted into the cistern and attached to a 1 millimeter bore water manometer. Six tenths cubic centimeter of cerebrospinal fluid was required to fill the system to starting pressure. The corneal and palpebral reflexes were evaluated by appropriate stimuli before and after injury. The state of consciousness was determined by the animal's response to tail and paw pressure stimuli. The morphinized animal would react to from 4 to 8 kilograms of tail

pressure, the unconscious animal showed no response to stimuli. Differing from the effects of barbital or other anesthetics, morphine clearly permitted recognition of unconsciousness.

Various mechanical devices were used to produce the injuries. These are shown in Figure 1. Injury to the fixed head was accomplished by a directed falling weight of 55 pounds and by hammer blows. The nonfixed head was struck by means of a hammer, by a hitting object propelled by a pendulum and also by a spring. High ranges of velocity were produced by the pendulum, the axis of which was eccentric serving to rotate 140 pounds of weight. The spring device was similarly able to develop high velocities by virtue of the type and position of the spring. Penetrating injuries were produced with gunshot and a mechanical drill. Twenty-two caliber bullets of varying velocity and size were employed. A mechanical drill was used to obtain a penetrating injury of minimal velocity. In a number of instances, gunshot wounds were made after disturbance of the closed cavity hydrodynamics by opening the cistern to expose the medulla, suboccipital craniectomy and unilateral or bilateral craniectomy to expose one or both hemispheres. Infiltration of 1 per cent procaine was used in these procedures for local anesthesia.

## DISCUSSION OF EXPERIMENTAL DATA

The injuries produced in this study were divided into three groups. The first group included animals injured by a falling weight or hammer blow striking the fixed head (30 experiments). The second group was comprised of animals which were struck by objects of graduated velocities applied to the nonfixed head. The origins of these forces were the hammer (26 experiments), pendulum (24 experiments), and the spring (20 experiments). The third group sustained injuries of a penetrating type including gunshot injuries (38 experiments).

The acute physiological effects and the pathological damage under these varying conditions were studied and correlated. Particular concern

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was given the state of consciousness, the corneal and palpebral reflexes, the respiration, the blood pressure, the intracranial dynamics, extensor phenomena, the convulsive state, the morbidity and the mortality. The resultant skull and cerebral injuries were classified according to the degree of changes produced.

Three levels of the physiological response to the cranial trauma were seen. These were (1) minimal (2) moderate (3) profound. The animals in the minimal group tolerated the injury with no significant changes in the vital functions of respiration, blood pressure, and reflexes. Animals in this group uniformly survived the acute injury. The moderate group included animals in which there occurred a cessation of the respirations or an interruption of the corneal and palpebral reflexes. A temporary rise in blood pressure was usually observed. The animals lost consciousness for variable periods of time. Animals in the moderate group were not all able to survive the injury. The profound group was characterized by the death of the animal during the acute experiment. Respirations and the corneal and lid reflexes were usually abolished. A remarkable (temporary) rise in blood pressure with tachycardia was a characteristic reaction. The animal was unconscious until its death.

The pathological damage to the brain could be classified into four groups irrespective of the mechanism of injury. These were group 1: no gross lesion but occasional slight congestion; group 2: cerebral contusions, grade 1 and 2; group 3: cerebral contusions, grade 3 and 4; group 4: brain laceration and contusions. The skull was fractured in all instances except when indicated in the various charts.

Forces of varying intensity applied to either a fixed or semifixed head were observed to produce physiological responses proportional to the degree of pathological damage to the brain. The attempt to produce profound physiological effects without producing pathological damage failed. The results of the injuries are illustrated in charts and described and discussed under subject heading.

#### THE CONSCIOUS STATE

An evaluation of the conscious state was made before and after each injury. The usual mongrelized dog was conscious before the injury occurred. Although this state was depressed, the animal could still respond to external stimuli of sensitive regions. Tail pressure was administered with a dynamometer and the level of response was recorded. Further depression or complete failure of response after the injury could be evaluated.

An attempt was made to produce unconsciousness without associated gross pathological change in the brain (concussion) since this is an interesting and controversial subject. It was possible to do this in but a few instances. In order to produce loss of consciousness, it was necessary as a rule, to produce cerebral contusions. The striking forces were varied in the attempt to produce not only concussion but concussion with resultant death of the animal. As shown in charts, Figures 1, 3 and 4, fatalities resulted only after injuries which were severe enough to produce high grades of pathological damage. Death from concussion did not occur.

Brief periods of unconsciousness and semi-consciousness were observed in the minimal groupings. Depression of the conscious state was the commonest finding. In the moderate group, consciousness was frequently lost for prolonged periods. In the profound class, the unconsciousness was uniformly followed by death.

The relationship of the conscious state after injury to the corneal and palpebral reflexes was studied. Analysis showed that a number of conditions were possible. Loss of consciousness frequently obtained with no changes in the reflexes. Loss of consciousness and loss of reflexes were frequently found together. In some instances the reflexes would then return while the animal continued in an unconscious state. A consistent finding without exception was that consciousness was never present during the period of reflex loss. The observations made it clear that loss of consciousness and loss of the corneal and palpebral reflexes did not represent the same level of response to injury.

#### RESPIRATIONS

The effects of cranial trauma were found to be intimately associated with the mechanism of respiration. In some instances pathological damage to the brain was produced without recordable evidence of any influence upon the respiratory activity. Application of forces producing moderate physiological effects usually resulted in cessation of respiratory function for variable periods of time. In a few instances the respirations were stimulated. The time interval of respiratory loss until recovery varied from a few seconds or a respiratory pause to losses for as long as 700 seconds. The cessation of this function was usually attended by an absence of the corneal and palpebral reflexes and unconsciousness. In the profound group, respirations were abolished completely and usually permanently. This was not a uniform finding permitting the conclusion that the respiratory centers were more vulnerable than



Fig 1 The devices used to injure the head, showing from left to right, the spring instrument, the falling weight, and the pendulum

other vital centers, that death occurs because the respiratory centers have ceased to function. Evidence to the contrary was found in the observation made a number of times that the respiratory activity returned but that the heart continued to fail in spite of renewed oxygenation. In other cases of temporary recovery of the respiratory centers, the onset of oxygen intake in the presence of a falling blood pressure was immediately revivifying. Rises and falls in the blood pressure then occurred synchronously with each respiration. Comparison of the vulnerability of the respiratory and reflex centers to trauma showed a wide variation in the response of each, illustrated best among the injuries in the moderate group. Absence of respiration for an interval comparable to the period of loss of the corneal and lid reflexes was commonly observed. Also frequent was abolition of the eye reflexes with no changes in the respiratory activity. In some instances the reflexes were lost for longer periods than the respirations.

#### REFLEXES

The activity of the lid and corneal reflexes mediated by the 5th and 7th cranial nerves offered a valuable index of severity of injury. In this respect, the minimal group were characterized by no changes in activity. In the moderate class, these reflexes were lost for periods which varied from a few seconds to  $6\frac{1}{2}$  minutes. Injuries resulting in a profound response were attended usually by loss of activity to the animal's death. In a few

instances there was a temporary recovery of function with secondary loss of activity. In our experience, loss of the lid and corneal reflexes represents a more profound response to trauma than unconsciousness.

The reflex of deglutition was found to react in the manner of other bulbar reflexes. Particular attention was given to this reflex in relationship to the unconscious states produced. It was noted that this reflex as well as the corneal and palpebral were frequently preserved in unconscious animals. Hopping and stepping reflexes were lost during unconsciousness. Deep tendon reflexes remained

#### BLOOD PRESSURE

A remarkable rise in blood pressure was usually observed after injuries in the moderate and in the profound classifications. The rise was prompt and reached levels of 300 millimeters of mercury. Tachycardia always accompanied the rise in pressure. In the moderate group, the maximum rise would be maintained over 60 to 120 seconds. In the profound group, the pressor effect continued usually through a period of 180 seconds and gradually failed to zero at the animal's death. There were some instances among the more severe injuries in which hypertension did not occur. It was notably absent when a crushing injury to the skull and brain was produced, in this circumstance, an immediate fall in pressure was sometimes noted. Strong vagal influences were frequently observed to interrupt the tachycardia.

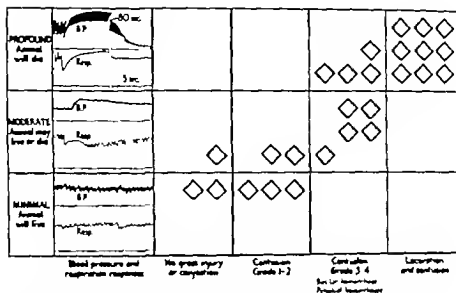


Fig. 2. Correlation of the physiological and pathological effects of injury to the head. Profound effects did not occur unless gross damage as produced.  $\diamond$  indicates falling body.

Study directed to defining the mechanism responsible for the hypertension showed that it could be prevented from occurring by section of the spinal cord at the first thoracic segment. These animals were prepared the day before injury and were then subjected to blows which resulted in profound effects without hypertension. Removal of both adrenal glands had no effect upon the pressor response after injury. Unobliterated animals, which did not respond to adrenalin, showed no rise in pressure following injuries of fatal intensity. The observations which we have made favor the conclusion that the activity of the sympathetic nervous system is the cause for the acute hypertension resulting from injury to the head. Measurement of the blood flow in the spleen and the hind paw showed a decrease in flow in the splanchnic distribution and increased blood flow in the hind paw. A similar dissociation of the blood flow in the splanchnic and peripheral circulations has been observed by Green and Hoff following stimulation of the cerebral cortex. Gun shot injuries, discussed under separate heading, were of particular interest in respect to the occurrence of hypertension at the time of injury. These injuries produced a uniform pressor effect similar to that noted in the low velocity nonpenetrating types of injuries. The hypertension could be prevented from occurring by a bilateral decompression of bone and dura mater. Injury to the medulla also resulted in absence of the pressor response.

The question may arise as to the rôle of the cortex in mediating or assisting in the pressor response. A remarkable rise in blood pressure after cortical stimulation has been recorded by Green and Hoff and Crouch and Thompson. Stimulation of the hypothalamus may also result in hypertension (7). The significance and rôle of the lower brain stem centers, however, has been clearly defined by Denny Brown and Russell who showed that the pressor response occurred in head injury after decerebration of the animal preparatory to injury.

#### INTRACRANIAL HYDRODYNAMICS

The spinal fluid pressure in most cases, was measured shortly after the production of the injury. A pressure was recorded usually in the range of between 50 and 200 millimeters of water. (The highest pressure observed was 300 mm.) These findings were similar to those previously reported (26). Others have not found but a small rise in the cerebrospinal fluid pressure after injury of the experimental (anal (6) and no significant change in the water content of the brain (20).

Blood was commonly noted in the spinal fluid. The degree of bloodiness was commensurate with the intensity of the injury in most cases. Increasing quantities of blood in the fluid were associated with correspondingly higher pressures, results being similar to those reported in detail (26).

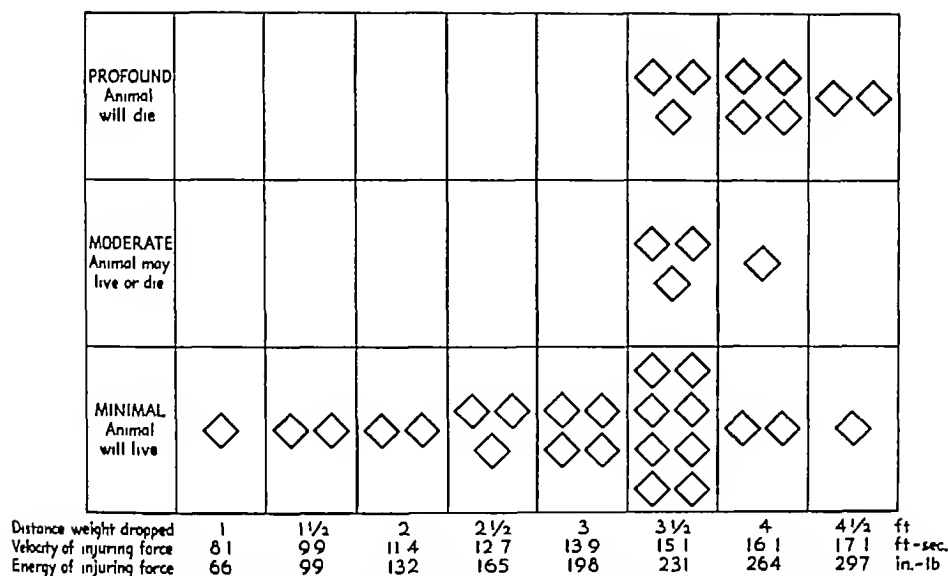


Fig. 3 Correlation of the velocity and energy of the injuries (5.5 pound weight) to the fixed head with the physiological effects ◇, Falling body

Injuries produced by gunshot wounds gave evidence of an intense increased intracranial pressure at the instant of injury. Such a pressure effect was visualized by exposure of the cisterna magna, at the moment of injury the cerebellum was extruded into the opening. A suboccipital craniectomy followed by a supratentorial, gunshot wound was observed to result in expulsion of the cerebellum with such force as to lacerate that tissue. A gunshot injury striking 5 centimeters below the medulla and transecting the cord resulted in cerebral contusions of the cortex of the hemispheres due possibly to transmitted high pressure. Cerebral tissue was consistently extruded through the defect made by a bullet's entrance. Measurement of the intracranial pressure at the time of injury by means of a fluid system, attached by copper tubing to a tambour from an adapter screwed into the skull, showed this instant qualitative change in pressure.

#### PATHOLOGY

The pathological findings were grouped according to the degree of injury to the brain and skull as previously noted. Brain injury was absent or there was congestion at the site of injury, in the animals of group 1, mild contusions graded 1 and 2 were present in group 2, severe bruising graded 3 and 4 was present in group 3, brain laceration and contusion were characteristic findings in group 4. Similarly the degree of bone deformation

was graded. A fine fracture was present in grade 1, linear but more extensive fracture in grade 2, depressed in grade 3 and comminuted and depressed in grade 4.

**Group I** The animals in this class showed no cortical damage. Congestion of the surface vessels at the point of injury sometimes occurred. Congestion was defined as present when the vessels were merely more prominent than in the normal brain. Cross sections of the brains showed no gross damage. Frequently a blanching of the bone was noted at the point of injury. In most cases a fine fracture occurred which was classified as grade 1. The injuries of this group occurred by the application of forces of the lowest intensity in the range used.

**Group II** The second group of pathological specimens were characterized by mild degrees of contusions which were labeled as contusions grades 1 and 2. Contusions were usually found at the site of injury. Frequently they were located over the temporosphenoidal lobe and on the tentorial surface of the occipital lobes. They were sometimes present opposite to the point of impact under conditions of both the fixed and nonfixed head. Cross sections of the brains of the animals in this group, as a rule, showed no microscopic changes. A grade 1 or 2 fracture of the skull was usually present. In some instances, contusions grades 1 and 2 were observed without an associated fracture of the skull. This degree of bruising was



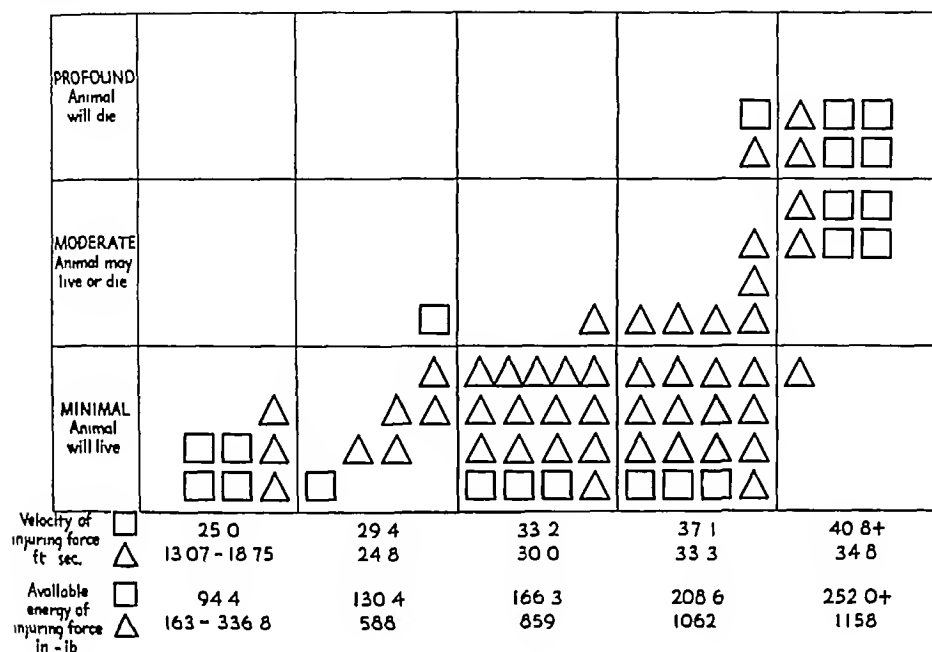


Fig 5 Correlation of the velocity and available energy with the effects of injury to the nonfluxed head. The animal's head was able to absorb the energy produced by the spring,  $\square$ . With the pendulum device,  $\triangle$ , much of the energy was expended into the stop bar after the head was set in motion.

tion Kramer and Horsley (16) reported that death "is not, as usually supposed, due to failure of the heart, but to arrest of the respiratory movements." The changes in circulation consisted of "(a) slight initial fall of blood pressure, (b) considerable later rise of blood pressure, (c) preservation of the rhythm of the heart."

The observations which we have made confirm those of Kramer and Horsley concerning the importance and vulnerability of the respiratory center in gunshot wounds of the brain. The response of the vasomotor center to this type of trauma was found to differ from that reported by these observers. In our experience, the rise in blood pressure was abrupt, profound, and uniform in the high velocity group of injuries. The rise began at the moment of injury, it was not preceded by a fall in pressure. There was an associated tachycardia and increased pulse pressure.

The lid and corneal reflexes were deranged in direct proportion to the severity of brain stem injury, as were the respirations and vasomotor activity. In the profound group, these reflexes and the respirations were abolished. In the minimal group, although minor disturbances of respiratory rate occurred, reflex function was normal to all appearances. Unpredictable reac-

tions of the vital mechanisms were observed in the moderate group. In some instances, respiratory activity alone was lost, the lid reflexes remaining active, in others, reflexes only were lost. In the largest group, both respiratory and reflex function were lost together and each recovered at varying and different periods. The absence of the lid and corneal reflexes was always associated with unconsciousness. However, unconsciousness was also found to occur in the presence of active lid and corneal reflexes. These phenomena were therefore similar to those observed after other forms of injury.

#### EVALUATION

Variations in the methods used to study head injury may account for the differing results and consequent conflicting viewpoints. The dog, cat, and rabbit have been mainly used in experiments on cranial trauma. The type of the animal, its age, the thickness of the bone of the skull, and the thickness of the masseter muscle are factors which can influence the responses to injury. In the dog, the masseter muscle, because of its development and attachment to the bone, provides a helmet-like protection. It is generally accepted that it is difficult to injure the dog fatally by means of blows to the head possibly due to muscle buffering.



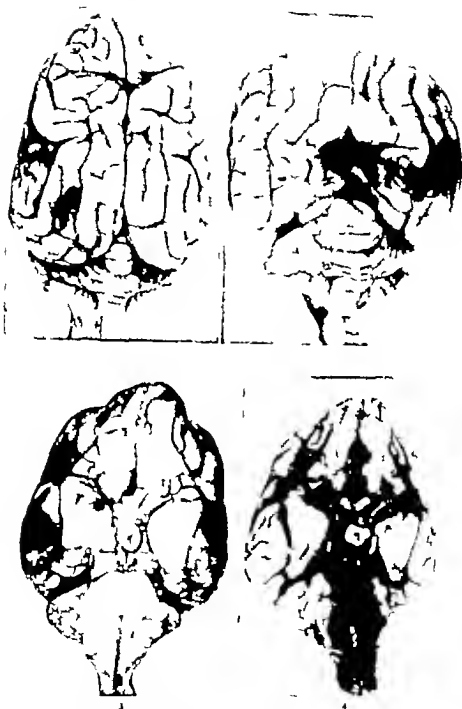


Fig. 6 Specimens illustrate the various degrees of pathological injury produced. Cerebral contusions are graded into 4 groups as indicated by illustration 2, 3, and 4.

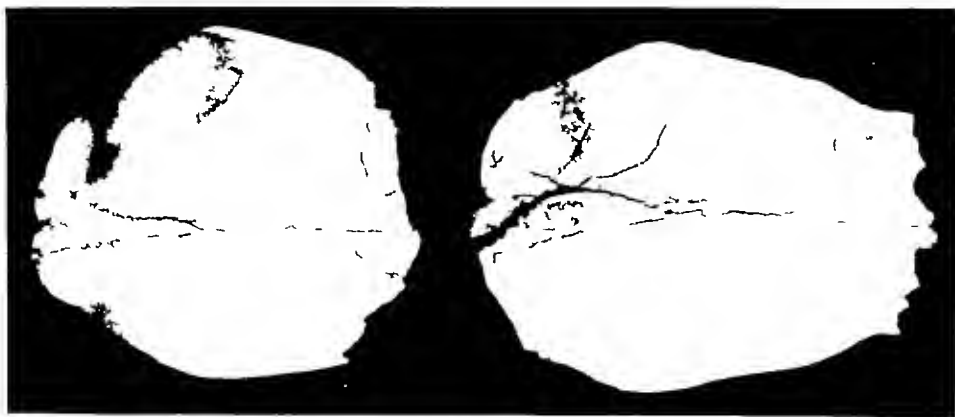


Fig 7 Examples of fracture of the skull grade 1, left, and grade 3 are shown

(1) Injury to the exposed skull or to the muscle protected skull may produce different effects. Various anesthetic agents have been used during the experiments, barbituric acid derivatives and ether being the most common. The effect of the anesthesia in its relation to the experimental results has not been critically analyzed. Such factors may account for the differences of opinions concerning the results of injury.

In the experiments upon dogs reported in this paper, an attempt was made to evaluate, as far as possible, the injuries under controlled conditions. For this reason, the selection of the type of anesthetic was held to be of first importance. Morphine analgesia was used since the state of consciousness could be readily recognized. Morphine does not influence the activity of the palpebral and corneal reflexes as may occur by the use of barbituric acid derivatives. In further interest of controlling the conditions of experiment, the site of injury was exposed in each instance to eliminate masseter muscle buffering. The variations in bone thickness and tensile strength could not be controlled. Measurements of the bone showed variations between  $\frac{1}{32}$  and  $\frac{1}{8}$  inch. Under these conditions the energies produced by the various striking devices usually resulted in predictable physiological and pathological responses. In the experiments, a correlation of the physiological and pathological changes was found to exist. Minimal, moderate, and profound physiological effects were associated with very slight, moderate, and severe pathological changes in the brain. That is, animals which were struck with sufficient force to produce changes in vital functions showed also gross pathological damage in the brain. If the force applied was insufficient

to produce observable pathological changes, there were then no significant effects noted in the reflexes, the respirations, or in the blood pressure. Both physiological and pathological effects were found to be proportional to the intensity of the injuring force which was allowed to strike the head, irrespective of whether the head was fixed or nonfixed.

In these experiments, a velocity range of from 13 to 40 feet per second was developed. When the head was allowed to move, higher velocities were required to cause a given injury, than if the head were fixed. An understanding of the physiological effects observed may be aided by a consideration of the mechanical forces involved.

#### DYNAMICS

The physical forces producing craniocerebral injuries may be grouped into four classes: (1) force applied to a relatively fixed head (direct blow, "compression"), (2) force applied to a nonfixed head which may move by the force (direct blow, "acceleration"), (3) force applied through the head in motion coming in contact with a nonmoving or slower moving object (indirect blow, "deceleration"), (4) a combination of the preceding circumstances.

Whether the head is fixed or allowed to move at the time of the blow and whether certain critical velocities are significant in relation to the morbidity and mortality may be determined by analysis of the experimental data and the underlying physical findings. In this regard, we may consider the question of the forces involved from two points of view, first, that of the work done upon the bone and the intracranial contents, second, the dissipation of momentum at the

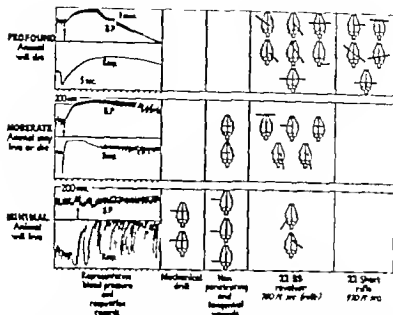


Fig. 8. A correlation of the physiological effect of penetrating and gunshot wounds of the brain, the type of penetration, and the elasticity of the brain object are shown.

instant of injury. In the circumstances of a fixed head, 55 pound weight was allowed to drop from varying heights to the exposed parieto-occipital bone. The object may be considered to be a free falling body. After the weight has made contact with the bone, it is ready to do work upon that bone. The amount of work that it will do is equal to its kinetic energy, a constant quantity for each distance dropped. The head being fixed, the striking object will cause a maximum of work done expressed by damage to the bone and the brain. All the available energy involved is completely dissipated as the weight is stopped by the unmoving head; whereas if the head is allowed to move part of the energy is dissipated in moving the head.

In the use of a pendulum, whose energies were derived from springs and a vector of the acceleration of gravity, a much greater capacity for work was developed since a greater kinetic energy was available in the instruments. With these devices, the head was allowed to move after being struck. Energy was delivered to the bone and intracranial contents through a longer time interval of contact with the skull. Unlike the conditions of a fixed head the energy was in part dissipated in moving the nonfixed head. It was dissipated also in the stop bars which were used in the spring and pendulum instruments. It is

evident that large velocities were needed in order to parallel the pathological damage obtained by the use of the unobstructed falling weight on the fixed head which did not move the head at striking.

The instrument or hitting object must have a certain quantity of mass before physiological damage may be produced. A relatively great velocity with an extremely small mass may produce minimal injury. Conversely, large mass with minimal velocity may produce no significant effect. The product of mass and velocity is momentum, a quality which all bodies in motion have. In our experience the acute physiological and pathological effects of a blow to the head are proportional to the time rate of change of momentum, within an optimum range.

A blow on the head may cause a local effect, a general effect, or a combination of local and general effects. Depending upon the severity of the blow and the dissipation of energy by buffering and deformation, the effect may be local and may result in bruising or laceration of the scalp, fracture or depression of the skull and bruising or laceration of the subjacent brain. If the energy is sufficient high, it may be transmitted to the contents of the skull, as set forth by P. Wolf's law. Lesions may be caused in the path of the direction of energy and others may also result in distant portions of the cranial cavity.

The general effects of a blow to the head are brought about by several factors. Among the more important are first, a sudden intense increased intracranial pressure at the moment of injury, second, mass movements of the brain at the time of the blow, third, cellular damage due to transmitted energy to the head with no accompanying increased intracranial pressure. Any of these factors, or a combination, may result in intracellular, microscopic, or gross disturbance of the intracranial structures.

1 A sudden intense increase in intracranial pressure may occur at the time of the injury and has been demonstrated by Kramer, Cannon, Kocher, and Scott. The increase in intracranial pressure may produce reversible or irreversible cell damage. The most vulnerable cells are involved with ensuing pathophysiological manifestations. The brain stem with its respiratory and vasomotor centers, which are most essential, may become stimulated or inhibited by trauma. Mechanical compression (5), application of electrical currents (17), chemicals and heat (10) to the medulla cause similar stimulation or inhibition of the medullary centers. The conclusions of Scott that the increase in intracranial pressure, lasting  $\frac{2}{10}$  seconds, produces ischemia, that the ischemia in turn results in unconsciousness and hypertension, are not warranted in the presence of strong evidence to show that unconsciousness due to anemia does not occur until 8 to 10 seconds have elapsed (17).

2 Mass movements of the brain may cause microscopic or macroscopic damage. In these observations mass movements occurred with the head fixed or nonfixed. A greater degree of damage occurred due to this cause when the head was nonfixed. Following a blow to the skull, the intracranial contents may abut against solid structures causing added damage. Similarly, the crowding together of the brain itself because of difference in density may result in parenchymatous lesions. Contrecoup lesions so common in head injury are ascribed to a lag of the brain behind the more rapidly moving cranium or there may be a "bouncing back" of the brain when the moving head is suddenly stopped by a nonmoving or slower moving object. Phenomena of "suction" and "sliding" of the brain have been described in connection with mass movements (23). In our experiments, the presence of contrecoup lesions on the surface of the brain opposite the area of impact suggests that the transmitted energy may travel in a given direction with abutment of brain against skull at the end of the path of energy (3).

3 Cell derangement may result from the transmitted energy to the skull contents without an increase in intracranial pressure. Energy which injures a brain may produce a "commotio cerebri" (1, 8, 18), "a shaking of the nervous system" (19), "a disturbance of cell equilibrium" (17, 22), "a vuleneration of the nerve cells" (12), "a molecular derangement" or "ebranlement" (13, 21)—terms used to describe a diffuse response of the intracranial structures at the time of injury. The result of the injury is directly proportional to the intensity of the energy acting upon the head, the result expresses the amount of "work done." Whether the head is fixed or nonfixed at the time of trauma is important in terms of work allowed or degree of dissipation of the momentum. The cellular disturbance may occur from a single application of an adequate quantity of energy or from multiple applications of energy of lesser intensity (21).

The acute physiological effect following a gunshot penetrating wound of the head in the experimental animal may be due, we believe, to the intense, momentary increase in intracranial tension at the instant of injury rather than to "a gradual rise in the intracranial tension due to hemorrhage within the skull cavity" suggested by Kramer and Horsley (16). This phenomenon of increased intracranial pressure was absent in penetration of the brain with a low velocity object. The force, known as "explosive force," of a high velocity bullet transmitted to a closed, semifluid system, resulting in a sudden, increased, intracranial pressure, is dispersed throughout, acts upon all tissue, is manifested by the response of the vital medullary centers. Vital cell or center injury, recoverable or fatal, may be the direct result of this sudden pressure. The indirect effects of intrinsic vascular damage plus the local destructive process may cause additional immediate or delayed injury to the cells. Mention only is necessary to indicate that injuries by extensive dissolution of the brain as well as those produced by extreme velocities were excluded from this study.

In summary, trauma to the head causes acute pathophysiological effects through visible and invisible damage to the intracranial structures in a manner outlined. Other known and unknown factors act in the interval between the application of the force and the recovery or death of the subject. Known factors include immediate or secondary vascular damage, hemorrhage, infection, gross tissue destruction by macerating low velocity objects or shattering high velocity shell fragments or bullets.

Unknown factors include chemical and physico-chemical processes which occur following trauma. Only meager efforts have been directed toward this line of investigation. Outstanding among these is the work of Cannon who studied the later or secondary effects of injuries and arrayed evidence to show that the forces of osmosis play a significant rôle in cell injury. It is reasonable to believe that factors of this order deserve recognition in the development of a full view of the subject of brain injury. This phase has not been included in the sphere of our present observations.

#### SUMMARY

1. Cranial trauma was produced in 150 non-phrized dogs under controlled conditions by varying the type and intensity of the injuring force.

2. A correlation was observed between the intensity of the injuring force or the work done upon the skull and brain and the physiological and pathological effects of injury.

3. A correlation was also found to exist between the physiological effect of injury and the degree of gross pathological changes produced. Death was not observed to occur without visible pathological damage being produced in the brain.

4. A remarkable sudden increase in blood pressure was usually noted in the moderate and profound classes of injuries. This phenomenon was often accompanied by loss of the palpebral and corneal reflexes, loss of respirations, and unconsciousness lasting for varying periods. Recovery or death occurred in the moderate, while death always occurred in the profound group of injuries.

5. Animals were observed to be unconscious with active palpebral and corneal reflexes. Loss of these reflexes represented a more profound response to injury than loss of consciousness.

6. Penetrating gunshot injuries of the brain resulted in acute physiological effects similar to those which were noted in other forms of trauma.

7. Injuries were produced to the nonfixed head with striking objects propelled by spring pendulum, and hammer within a range of velocity from 3 to 40 feet per second. Higher velocities were required to produce pathophysiological effects under the circumstances of the nonfixed head than the fixed head. Whether the head was fixed or nonfixed the time of injury was important to

the extent of the work allowed upon the skull and contents, that is, at a given velocity the pathological and physiological damage was less marked if the head were allowed to move. However a greater degree of mass movements of the brain may occur under conditions of a nonfixed head.

8. The total acute effect of cranial trauma is due to a number of factors which includes: (1) sudden intense increase in intracranial pressure at the instant of injury; (2) mass movements of the brain; (3) a diffuse cellular disturbance due to transmitted energy with no accompanying increased intracranial pressure.

#### REFERENCES

- REFERENCES BY CANON (Cited by J. F. McGuire)  
Cited by SHAW and G. H. Arch. New Psychol., 1934, 3, 801.
1. CANNON, W. B. *Am. J. Physiol.* 1902, 6, 91.
  2. COCHRAN, C. B. *Arch. Surg.* 1917, 45, 9.
  3. CROOK, R. L., and THORNTON, A. *Anal. Rec.* 1935, 64 (suppl.).
  4. CROOK, R. L. *Brit. Johns Hopkins Hosp.* 1935, 100.
  5. DENT, BROWN, D. and RUSSELL, W. R. *Brit. J.* 1935, 64, 95.
  6. ECHOLS, L. *Am. J. Physiol.* 1917, 19, 307.
  7. GALE, Cited by Folia, A. *Rev. Chir. Par.* 1934, 4, 73.
  8. GREEN, H. D. and HOFF, F. C. *Am. J. Physiol.* 1937, 8, 611.
  9. HODGSON, E. S. *Am. J. Physiol.* 1937, 8, 30.
  10. HODGSON, E. S. *Brit. J.* 1935, 33.
  11. JEFFERSON, G. *Brit. M. J.* 1935, 807.
  12. KOCK, H. and FLEISCHER, W. *Arch. Chir.* 1934, 7, 60.
  13. KOCKER, T. *Hydrocephalus (Volkswagen) Arch. Path. Therapie* 1934, P. 320. Vienna: Alfred Holder.
  14. KRAMER, S. P. *Arch. Surg.* 1934, 1, 183.
  15. KRAMER, S. P. and HODGSON, E. S. *Proc. R. Soc. Lond.* 1934, 55, 278.
  16. MILLER, G. G. *Arch. Surg.* 1937, 4, 301.
  17. PARET, A. *Ouvrages complètes d'Ambréose Paret* ed. Malgaigne, Paris. J. B. Baillière, 1900, 21.
  18. PETIT, J. L. *Traité des maladies chirurgicales* Paris, 1774. Cited by Folia, A. *Rev. Chir. Par.* 1934, 4, 773.
  19. PILGRIM, C. *Arch. Surg.* 1937, 35, 3-377.
  20. POIRY, A. *Rev. Chir. Par.* 1934, 4, 374.
  21. RABIN, H. *Zbl. Chir.* 1930, 47, 46.
  22. ROWENHURST, G. F. *Acute Injuries of the Head* P. 1. Baltimore: Williams & Williams, 1935.
  23. SCOTT, W. W. *Arch. New Psychol.* 1934, 43, 279.
  24. TILLMANN, *Arch. Chir.* 1934, 59, 35.
  25. WHEATLEY, J. E., and FREEMAN, E. *Arch. Surg.* 1934, 3, 552.

# EDITORIALS

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## BACTERIA AND THE SURGEON

**S**URGLONS are constantly encountering problems of sepsis, asepsis, and antisepsis. In spite of this fact, there are too many surgeons who know too little about bacteria and their habits. Frequently they take cultures from wounds or exudates but pay little or no attention to even the laboratory report of the findings, let alone making any practical use of it. Too often, they regard the bacteriologic problem as being an academic one, apart from the clinical aspects of the case, something for the laboratory technician to work out, and for the hospital superintendent to report in the analysis of cases. This, of course, is not true, for the whole science and art of surgery depends so greatly on bacteriology. Without asepsis, practically the whole field of elective surgery would collapse. The intelligent care of infected wounds demands a thorough knowledge of bacteria, how they grow or how they may be inhibited. Who is in a better position to make contributions in

this field than the surgeon who sees and dresses the wound, or who opens and drains the abscess, and follows the clinical progress of the patient? Certainly not the laboratory technician or the bacteriologist whose chief interest is often concerned with the staining reactions of the organism, its reaction to culture media, to oxygen tension, and other similar qualities which allow it to be diagnosed and classified.

It is well known that many of the problems in surgical bacteriology have been solved by surgeons who are also trained bacteriologists. To mention only a few, one immediately thinks of the sterilization and standardization of catgut, the use of zinc peroxide by Meleney in the treatment of certain types of burrowing, progressive ulcerative lesions, and the use of high titered bacteriophage in the treatment of staphylococcus septicemia. Many studies on such matters as tetanus and gas bacillus infections have been made and are still being made by surgeon bacteriologists.

During the past few years, the development of the sulfone compounds and their use locally and systemically have further demoralized many surgeons, who now believe that throwing some of the "magic powder" into wounds and body cavities relieves them of further responsibilities, and if infection then develops or persists it is a sad trick of fate and no fault of theirs. Nothing could be farther from the truth. Many wounds heal more kindly without these drugs if adequate care and toilet of the wound are carried out. In this war, as in the last one, great emphasis has been placed on the healing of traumatic wounds and the best way to manage them. While many an average surgeon believes that he knows the best way, many experts are not so satisfied

that they do. They are studying with great care the results of various methods with and without débridement with and without closure, with and without sulfone compounds, etc. Careful cultural studies of tissue obtained by débridement such as those made by Altemeier throw considerable light on the subject and value of this procedure. Discussion with many surgeons by the writer has convinced him that débridement is employed very differently by different operators and that what one man regards as a careful and thorough débridement would be considered as inadequate by another. The problem of the man-

agement of traumatic wounds including burns, still has to be considered as an incompletely solved problem, for while these lesions today are treated better than they have been in the past, one has only to look at the multiplicity of methods advocated to realize that the ideal treatment has not been achieved. There is, therefore still ample opportunity to make contributions in this field of medicine and the surgeon who is willing to make use of the existing bacteriologic knowledge in his care of wounds should be in the best position to help in solving this problem.

M. M. ZIMMERMAN.

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

ALL of the contributors to the first edition of Morris' *Human Anatomy*<sup>1</sup> were Englishmen, associated with hospitals in or near London. The volume was originally designed for the use of students "preparing for the Conjoint Board of the Royal Colleges of Physicians and Surgeons, for the Fellowship of the Royal College of Surgeons," etc. The contributors to the current 10th edition are 12 Americans, who hold, or have held, professorial appointments in anatomy, in medical schools of the United States or Canada, no one of the original authors of the work, first published almost 50 years ago, is on the present list.

Editorship of the present edition was assumed by Professor Schaeffer after ill health required Professor Jackson to withdraw from such duty. As the editor's preface records, death has removed Professors Bardeen, Senior, and Stoeckard from the list of contributors, while Professor Hardesty has retired from activity associated with the new edition. These earlier contributors have been replaced by Professors Grant, Patten, Cummins, and Larsell, in the preparation of the sections on the musculature, the cardiovascular system, the skin (and special glands), and the nervous system, respectively.

Several sections of the treatise have been profoundly altered in rewriting, others have been rather moderately changed. Many of the older, inadequate figures have been replaced, chiefly by borrowing extensively from impeccable foreign sources. The sectional lists of important bibliographic references have been extended, an improvement which should be welcomed by all teachers and advanced students of gross anatomy.

The first section, on developmental anatomy, while actually shorter than it was in the prior edition, is nevertheless far more informative, since descriptive material has been converted into series of schematic figures. Professor Scammon has made each set self contained and, through ingenious labeling, virtually self-explanatory. By this means the general developmental history of viscera, skeleton, and nervous system, to name but several items, is managed graphically. The 2d section, dealing with the skin and its modifications, has been rewritten by Professor Cummins, with additions to text and illustrations. The 3d and 4th sections, on osteology and articulations, by Professor Terry, have been made more readable through being set up in regular type, the use of fine print has been reduced to a minimum. In the form revised by Professor Grant, the 5th section,

on musculature, has been slightly lengthened, major descriptive material on origin, form, course, and insertion of muscles is set up in regular type, an arrangement convenient to the student who must read his book at the dissection-table, descriptions of action, relations, and variations are in fine print. In general the subject matter is fortunately presented in the critical form composed by the late Professor Bardeen. The 6th section, on the cardiovascular system, enlarged by Professor Patten, retains much of the textual substance of its predecessors, but is greatly improved by the new account of morphogenesis and variations of the vascular system which is illustrated by diagrammatic figures. Many new colored figures have been added, borrowed from the Tandler *Lehrbuch*. The 7th section, dealing with the lymphatic system, by Professor Clark, remains essentially the same, as does section IX on the special sense organs by Professor Arey. These chapters, thoroughly revised for the earlier edition, required little alteration. In the 8th section rewritten by Professor Larsell, is contained the bulk of the neural material presented in earlier editions but modernized through additional detailed descriptions on nuclear masses and tracts, and accompanying diagrams. The 9th section by Professors Jackson and Blount contains numerous new and helpful illustrations, and the older ones are improved. The text contains concise accounts of recent researches, affecting, among other areas, the gall bladder and biliary ducts. These statements also apply, generally, to the 11th section on the respiratory system, by Professor Schaeffer, and to section XII, by Professor Johnson, on the urogenital system. In the 13th section, by Professor Gudernatsch, on the anatomy of the glands of internal secretion, new figures have been added and the text has been brought up to date.

The volume is about 100 pages longer than it was in the prior edition, but the added bulk has been most advantageously used. The descriptive material has been printed in type of easily readable size. The work continues to be encyclopedic, in the traditional manner, it contains, to approximately one-sixth of its bulk, material that is nowadays handled admirably by the separate textbooks of embryology, neurology, and histology.

BARRY ANSON

THE ever increasing incidence of malignant disease throughout the civilized world and the equally increasing occurrence of hazards of industrial life as well as those associated with the average trend of modern living, many apparent and controlled and many not, suggest a study of a possible relationship. Studies have been made of carcinogenetic sub-

<sup>1</sup>MORRIS' HUMAN ANATOMY. A COMPLETE SYSTEMATIC TREATISE. Edited by J. Parsons Schaeffer, A.M. M.D., Ph.D. Sc.D. 10th ed. Philadelphia: The Blakiston Co. 1942.



stances, their tractate determined and their occurrence in matter that may come in contact with the human body established. Also many apparently benign substances have been studied with the view of determining the presence of carcinogens. Many of these reports are inaccessible and appear in scattered journals throughout the world. To answer this pertinent problem, compilation of factual information on the subject of tumors of occupational origin has been prepared by H. eper.

The casual student of the subject cannot realize the enormous amount of work that has been done on the problem. The average physician as an example is aware of tar as a causative agent in the production of experimental cancer; however he has not the slightest conception of the tremendous amount of study that has been given the subject. This is well exemplified in this new work. Here under tumors of the skin the author considers of the organic chemicals

the distillation and fractionation of coal, oil shale, lignite, bitumen, goodron, asphalt, crude mineral oil, and similar naturally occurring substances. To this is devoted some 300 pages. Such details as distribution, chemical and technological aspects, historical and geographical aspects, exposure and incidence, symptomatology, site, multiplicity, prognosis, age, duration of exposure, sex, cohabitation, latency period, acute traumatic tar cancer, histopathology, experimental tar and pitch cancer, causative mechanism, and technical, sanitary and medical protective aspects are considered. For those interested in these substances the low and high temperature distillations ranging from 51 to 300 degrees C are discussed.

Chapters are devoted to concepts and significance of occupational tumors, occupational and accidental tumors of the skin and its appendages, the alimentary system, respiratory system, the urogenous organs, hyperplasia and neoplastic diseases of the blood-forming organs, tumors of the mesenchymatous tissue, the eye and its adnexa, the nervous system, the endocrine glands, the sex organs, special aspects of occupational tumors, the relationship of occupational neoplasia to the theories of carcinogenesis and medicolegal and public health aspects.

This work contains such an enormous amount of information that it is beyond the scope of review to describe the contents. It is fascinating reading for one interested in the subject of tumors or industrial hazards. Because of the pathological associations, more is included than the problem of neoplasia. The chapter devoted to the alimentary system can be found an extremely interesting survey of cirrhosis of the liver. The chapter on the respiratory system is timely and pertinent in view of the fact that cancer of the lung has become so prevalent during the past decade or two. The same comment may be made on the chapter on the urogenous system because of the impression that bladder carcinoma is definitely increasing. At the conclusion of each chapter is appended an extensive bibliography.

There has been accomplished the aim expressed in the above in the preface. It is the principle aim of this book to furnish an extensive source of information concerning the various aspects and the different types of these people's disorders which have come to claim an ever-increasing importance part of the problems of cancer in general. A reference book is now offered in which the pertinent data, often not readily accessible and widely scattered in journals, have been compiled. An attempt is made to analyze critically and to integrate the evidence obtained from different sources, and to correlate and evaluate the various observations and theoretical conceptions advanced, so as to form a well balanced and when possible, coherent picture of the subject under discussion.

This work should be of special value to every physician to governmental and legislative groups dealing with public health problems, and to the industrial employers. The author must be congratulated upon the completion of such an enormous task and his evaluation of the compiled data.

JOSEF W. LOURIE

THE 31st edition of *Physical Diagnosis* by Richard C. Cabot and F. Denettie Adams scarcely needs introduction to most students of medicine as this volume has been used throughout most of its editions as a standard text.

Adams collaborated in a complete revision of this book in the 18th edition. The present edition has again been extensively re-edited. The volume much larger and more complete than earlier editions. It contains a text of 833 pages with full and detailed index of 53 pages.

The material presented is primarily the teaching views and standards of the medical history and physical diagnosis upheld by the staff of the Massachusetts General Hospital. In addition accepted clinical procedures presented in the current literature are given.

The purpose of the book has been expressed by the author in the preface as follows: "To show how to think the patient should be examined to describe and interpret important symptoms and signs, and briefly to discuss the more common disorders in which they occur."

Which they occur. Strict adherence to this policy makes the volume useful as a reference text of differential diagnosis.

A criticism concerning the propriety of including discussion of clinical entities in a basic book of physical diagnosis has been capably answered in the preface. The author states: "I can only emphasize again, my conviction on which the 31st edition is based, that physical signs can be intelligently taught and intelligently learned only in their relationship to, and apart from the other aspects of disease. If this concept is borne in mind, certainly the approach and plan of the text are fundamental sound."

PHYSICAL DIAGNOSIS. By Cabot and Adams. 31st ed. by F. Denettie Adams. W. B. Saunders. The Williams & Wilkins Co., 1942.

The section on cardiovascular disease follows the Massachusetts General Hospital etiological classification, which the author admits is incomplete. It is unfortunate that the classification of cardiac disorders of the American Heart Association has not been included, or at least, presented for discussion.

The format of the book, as in previous editions, is excellent. The plan of presenting the subject by anatomic systems of necessity involves repetition of certain disease entities in the discussion. This, however, is effective and well tolerated by the reader.

I believe this volume will be found more practical than previous editions, not only for medical graduates, but also for the student just beginning his studies in clinical medicine. EUGENE L. WALSH

BECAUSE of its general plan, the broad field covered, and the excellence of the individual papers the 3d volume of the *Medical Progress Annual*<sup>1</sup> should be of interest to every clinician. It serves as an admirable "Year Book" of value not only to the specialist but also to general practitioners, internes, and to 3d and 4th year medical students.

The book consists of 52 articles that have been reprinted from issues of the *New England Journal of Medicine* for 1941. These articles represent the efforts of well qualified writers to cover recent advances in diagnosis and treatment in various fields, either in a general way or as they apply to some particular aspect of the specialty. The improvements in medical practice that, in the opinion of the authors, have been accepted and should be utilized are stressed. The list of references at the end of each article should be particularly helpful. A subject index is provided. Subjects of special interest to surgeons include general anesthesia, diagnostic roentgenology, operative technique, shock, transfusion reactions, surgery of the abdomen and of the sympathetic nervous system, thoracic and neurosurgery, radiation therapy in gynecology, treatment of pneumonia and of biliary tract disease. WALTER H. NADLER

THOUGH in the title of *4 Short History of Cardiology*<sup>2</sup> by Herrick the word "short" is used the outstanding and essential developments in the knowledge of the heart since the time of Harvey (1628) are adequately described in the volume. A short chapter, introductory in character, is given to the scant knowledge of the heart prior to the time of Harvey, Hippocrates, Galen, and Vesalius with a short notice of Leonardo da Vinci, whose interest was confined to anatomy, are discussed in the first chapter. Three chapters entitled "Harvey to Laennec," "Laennec to Virchow," and "Virchow to Pasteur" make up the most of the book. Shorter chapters entitled "Inflammation of the Heart," "Affections of the Myocardium," "Syphilis of the Heart and Aorta," and

<sup>1</sup>MEDICAL PROGRESS ANNUAL VOL. 3 1942 A SERIES OF FIFTY TWO REPORTS ON THE RECENT ACCEPTED ADVANCES IN DIAGNOSIS AND TREATMENT. Published during 1941 in The New England Journal of Medicine. Robert M. Nye Managing Editor. Springfield Ill and Baltimore Md. Charles C. Thomas 1942  
<sup>2</sup>4 SHORT HISTORY OF CARDIOLOGY By James B. Herrick. Springfield Ill. and Baltimore Md. Charles C. Thomas 1942

"The Coronary Artery and its Diseases" make up the rest of the book.

The author has presented a comprehensive and interesting story of the gradual development of our knowledge of cardiac disease. While presenting the history of research in cardiac disease, the author portrays the characters of many physicians from many lands, whose pioneer work is presented. Dr. Herrick has a gift for appraising his characters concisely and accurately, the facts of scientific investigation are made more interesting in the light thrown upon them by one who belongs to the inner circle of medical research. The author found time to portray the characters of the more important investigators, he tells not of science alone but of personalities. He has described the various approaches to research in times of ignorance and the tenacity which most of the investigators needed to maintain their discoveries. For instance, he gives some 15 pages to Bouillard, whose thorough work resulted in the demonstration of the relationship of acute rheumatic fever to cardiac disease.

The book is adequately bound and well printed. It will delight the members of our profession who are especially interested in cardiac disease, it will intrigue the physicians who are interested in medical history, the descriptions of the clinical studies and investigative procedures in widely different times may be read with pleasure and profit by the medical profession but also by many from every walk of life who are interested in the history of science as well as medicine. JAMES G. CARR

ANY writer who undertakes the herculean task of compressing into a single volume the enormous body of knowledge connoted by the title *Human Pathology*<sup>3</sup> deserves respectful consideration, even though complete success is impossible. Dr. Karsner acknowledges the book's limitations when he says in his preface to the first edition "A textbook is only an introduction to the essentials of a subject." The book has been popular as the appearance of 6 editions in 16 years well demonstrates. The material is presented in the pattern generally accepted as best designed for the instruction of medical students, dealing first with general topics and later taking up systemic pathology. In this latter division the author demonstrates the breadth of his knowledge by including many topics of interest to surgeons which are slighted or omitted in several other well known textbooks on the subject. The present edition contains much recent material and new references so that one can rest assured that revision has been painstaking and judicious.

There are omissions which are common to most textbooks of general pathology. There are, for example, no chapters devoted to the eye, the ear, and the skin. Perhaps this can be justified for the eye and ear, but the skin must be reckoned with by almost every physician, and surely some familiarity

<sup>3</sup>HUMAN PATHOLOGY By Howard T. Karsner M.D. 6th ed. Philadelphia Montreal and London J. B. Lippincott Co. 1942

with its pathology is essential for intelligent practice. The question of emphasis and space allotment

III. Of meet with a liberal agreement inevitably it could not do so for each one of us has varying ideas about which are the more important lesions. On the whole Dr. Kanner has done a good job and where lesions are only mentioned and not described, judiciously selected references enable one to seek more detailed information.

The illustrations are clear and usually illuminate the text instead of obscuring it, as is the case in some books. The type is good and easy to read and ref-

erences are up to date. An incomplete index, which delays one in finding some topics is the only mechanical defect to be found in an otherwise carefully prepared text.

This textbook can be recommended to medical students as one of the best single source general pathologies. For graduates in medicine it will be useful as a book of reference and for its bibliography. The surgeon will need more detailed knowledge of the pathology of the diseases which he treats to supplement the information contained in this volume.

ARTH. PRATT SPOFFORD

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

I SURGERY OF THE EAR. By JOSEPH A. REDMOND, M.D. Philadelphia and New York: J. B. Lippincott Co. 942.

THE PRINCIPLES OF PRACTICE OF OBSTETRICS. By JOSEPH B. DELEE, M.D. and J. P. GREENHILL, M.D. 8th ed. Philadelphia and London: W. B. Saunders Co. 943.

BURNS, SCALDS, WOUND HEALING AND VASCULAR INJURIES. Prepared under the auspices of the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Philadelphia and London: W. B. Saunders Co. 944.

ILLUSTRATIONS OF SURGICAL TREATMENT: INSTRUMENTS AND APPLIANCES. By ERIC L. FARQUHARSON, M.D. F.R.C.S.E., Major R.A.M.C., with foreword by Sir JOHN FRASER, M.C., M.D. Ch.M., F.R.C.S.E. 2d ed. Baltimore: The Williams & Wilkins Co. 945.

OBSTETRICAL PRACTICE. By ALFRED C. ROCK, M.D. 3d ed. Baltimore: The Williams & Wilkins Co. 946.

DISEASES OF THE NOSE, THROAT AND EAR, MEDICAL AND SURGICAL. By WILLIAM LINCOLN BAUBERGER, M.D., F.A.C.S. and HOWARD CHARLES BAUBERGER, M.D., F.A.C.S. 8th ed. Philadelphia: Lea & Febiger. 947.

SKIN IN STRUCTURE AND FUNCTION. By FRITS KAKA. Translated from the German and edited by GEORGE KOWEN, M.D. New York: Alfred A. Knopf. 948.

THE PRINCIPLES OF PRACTICE OF WAR SURGERY: ITS REFERENCE TO THE BIOLOGICAL METHOD OF THE TREATMENT OF WAR WOUNDS AND FRACTURES. By J. TRUETA, M.D. with introduction by OWEN H. WAGNERSTEEN, M.D. St. Louis: The C. V. Mosby Co. 949.

ESSENTIALS OF PROCTOLOGY. By HARRY E. BACON, B.S. M.D. F.A.C.S. F.A.P.S., with an introduction by CURTIS ROBERT B. L., M.D. F.A.C.S., F.A.P.S. Philadelphia, London, Montreal, J. B. Lippincott Co. 950.

PANCREATITIS ACUTA; APOPLEXIA OF THE PANCREAS; ARTERIOLE ARTERIO-SPERMATODERMIS OF THE PANCREAS; SPERMATODERMIS ACUTA; SPERMATODERMIS OF THE PANCREAS. By ULRICH R. ALBRECHT, M.D. New York & London: J. B. Lippincott Co. 951.

ORAL AND NOSE SURGERY. By EDITH L. LEWIS, M.D. St. Louis: The C. V. Mosby Co. 952.

REPAIR OF THE SOLA DUCTUS. By JAMES G. GIBSON, M.D. with preface by FREDERICK L. LONG, M.D. New York and London: D. Appleton-Century Co. 953.

GYNACOLOGY: WITH SECTION ON FEMALE UROLOGY. By LAWRENCE R. WHARTON, Ph.D. M.D. Philadelphia and London: W. B. Saunders Co. 954.

NEUROPATHIES AND THORACIC SURGERY. Prepared and edited by the Subcommittee on Neurosurgery and Thoracic Surgery of the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Philadelphia and London: W. B. Saunders Co. 955.

SYMPTOMS OF DISEASES OF THE SKIN. By RICHARD L. SETTON, M.D. and RICHARD L. SETTON, J. M.D. St. Louis: The C. V. Mosby Co. 956.

DOCTOR IN THE MARTIN. THE ART OF BEING A MEDICAL STUDENT. By ARTHUR W. HARR, M.B. and M.D. SEITZ, M.A., Ph.D. Philadelphia, London, Montreal, J. B. Lippincott Co. 957.

NEURALGIA ACUTA; THE STORY OF THE ARMY AND THE CORPS. By COLONEL JULIA O. FLECK, U.S.A., with an introduction by LT. COL. L. L. GARDNER, M.C., U.S.A. Philadelphia, New York, and London: J. B. Lippincott Co. 958.

# SURGERY

## GYNECOLOGY AND OBSTETRICS

*An International Magazine, Published Monthly*

VOLUME 76

JUNE, 1943

NUMBER 6

### THE SURGICAL MANAGEMENT OF SOME OF THE MORE COMPLICATED PROBLEMS OF PEPTIC ULCER

FRANK H LAHEY, M D , F A C S , and SAMUEL F MARSHALL, M D , F A C S ,  
Boston, Massachusetts

IN the last few years the surgical management of a chronic callous ulcer of the stomach and duodenum which fails to respond to conservative treatment has been established on a sound and quite universally accepted basis. Out of a confusion of conflicting opinions, definite indications for surgery have been outlined repeatedly and accepted by the majority of the medical profession. The need for adequate subtotal resection of the stomach for most chronic intractable ulcers is generally conceded. Furthermore, it is conceded that the likelihood of recurrent ulcer distress is reduced to a reasonable minimum by this operation and that recurrent ulcer, while it may occur, is infrequent after a properly executed resection of the stomach.

In this paper, our interest is not in these now recognized generalizations but in some of the more troublesome and complicated problems which arise in gastric and duodenal surgery as well as some of the conditions which follow a previous conservative or radical surgical procedure. In this complicated type of case the surgeon's experience and judgment may be taxed to the utmost, and he is apt to be faced with conditions producing the highest mortality rates in gastric surgery. He must acquire not only considerable technical ex-

perience with gastric surgery but he must also develop experienced surgical judgment with cases of this type if he wishes to avoid serious fatality percentages.

Since we have standardized the procedure at the Lahey Clinic, the risk accompanying resection of the stomach for the average duodenal, gastrojejunal, or gastric ulcer exclusive of gastrojejunocolic fistula is now reduced to 2.7 per cent. However, one cannot assume an attitude of complacency toward fatalities in this technically difficult group of cases, and so we have been interested in developing methods of surgical approach which will retain the risk at a minimum level.

The Clinic has had under hospital management 7,000 peptic ulcer cases, of which 6,550 were duodenal ulcers and 450 were gastric ulcers. Of this group of 7,000 peptic ulcer cases, 18.1 per cent of the gastric ulcer cases and 6.59 per cent of the duodenal ulcer cases required surgery for the relief of symptoms.

This paper deals with the complications in the last 251 consecutive patients who had subtotal gastric resection for peptic ulcer of various types. It includes subtotal gastrectomy for 152 duodenal ulcers, 45 gastric ulcers, and 46 jejunal ulcers in which were 8 gastrojejunocolic fistulas. There were 8 post-operative deaths, an operative mortality of

From the Department of Surgery, The Lahey Clinic, Boston.

3.1 per cent which includes the mortality of gastrojejuno-colic fistula. Of these 5 were patients with primary duodenal ulcer 2 were patients with gastrojejuno-colic fistula, and 1 a patient with a recurrent ulcer after subtotal gastrectomy.

The ulcer states which have been complicated and difficult to manage are the low duodenal ulcer involving the common bile duct in its indurated scar the ulcer located at or below the entrance of the common duct in the duodenum the gastrojejunal ulcer the gastrojejuno-colic fistula, and the recurrent ulcer in the gastric stump after a high subtotal gastrectomy. All the deaths among the 251 patients subjected to total or subtotal gastrectomy for ulcer with the exception of 1 patient who died of embolus, occurred in patients having ulcers of these complicated types. Two were patients with duodenal ulcer involving the common duct 2 were patients with an ulcer below the level of the point of entrance of the common duct into the duodenum 2 were patients with a gastrojejuno-colic fistula, and 1 a patient with a large recurrent ulcer in a gastric stump, the ulcer being of such size as to occupy practically the entire gastric stump and to require total gastrectomy.

In the surgical treatment of a patient with a duodenal ulcer for whom subtotal gastrectomy is contemplated, the first objective should be to expose the common duct and to settle its relationship to the level of the ulcer in the duodenum. To select the correct type of operation, one must first decide whether after removal of the ulcer with that part of the duodenum which it involves a sufficient amount of duodenum will remain above the sphincter of Oddi to permit safe inversion of the duodenal stump without obstruction of the entering bile duct. We have occasionally found a duodenal ulcer so low that after removal of the involved portion of duodenum, unless some measure was instituted to prevent its safe inversion of the cut end of the duodenum would occlude the entering bile ducts (Fig. 1a). In such cases it is advisable to open the common duct low and to insert a T tube with one long limb passing through the sphincter (Fig. 1b). This not only keeps the bile sphincter open until the duodenal stamp

heals and prevents jaundice from pressure of the inverted duodenal stump on the entering common duct (Fig. 1c) but also makes it possible to be sure of the relation of the retro-duodenal portion of the duct to the ulcer.

If the duodenal ulcer is actually below the level of the papilla of Vater as in 1 patient in whom death occurred after an unwise decision by one of us (F. H. L.) to employ subtotal gastrectomy excision of the ulcer with the involved portion of the duodenum should not be undertaken but rather a gastroenterostomy or a Finsterer resection by exclusion (Fig. 2).

If the duodenal ulcer is close to or in contact with the common duct it is here that the most experienced judgment is necessary (Fig. 3). In a written discussion a differentiation between a removable ulcer of this type and one which should not be removed is difficult. The distinction is clear to those who have dealt with a considerable number of duodenal ulcers, but it is not easy to make for those who are relatively inexperienced with these cases.

One sees two types of duodenal ulcer adherent to the common duct that type which consists largely of dense but flexible and movable scar tissue and that type which consists of a mass of firm inflexible white scar tissue of thick consistency and light in color. Removal of the latter gristle-like type of ulcer whether or not it invades the common duct, should usually not be undertaken as it frequently cannot be done safely. Ulcer erudate of this latter type is of such cartilage like consistency that it cannot be separated anatomically from the duct or other adjacent anatomical structures, and in addition in its separation one can so tear up the pancreas as to make possible a complication which can produce a fatality—pancreatitis. In the other type in which the flexible scar and adhesions about the ulcer have occluded the duct, removal can be undertaken safely.

The natural downward approach to the duct in separating the common duct from the scar and erudate of the ulcerated duodenum from the ulcer is not the best one. If one attempts to separate the duct from the ulcerated duodenum from above downward through the scar it is difficult not to make an opening into the duodenum and thus destroy

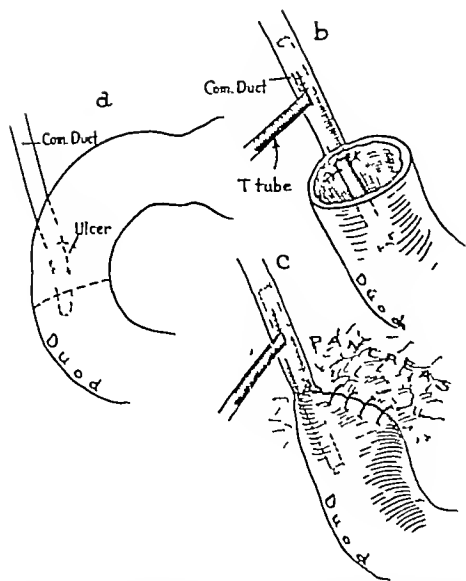


Fig 1 a, The relationship of a posterior wall ulcer adherent to the common duct and close to the point where that duct enters the duodenum. As indicated by the transverse dotted line, the ulcer is so close to the point of entry of the common duct that it may be necessary to transect the duodenum at a dangerously low level in order to get the ulcer out. b, The close relationship of the sphincter to the cut edge of the duodenum when it is necessary to transect the duodenum low as in a. A method of decompressing the common duct by inserting a T tube with its distal end projecting into the duodenum. c, The closed end of the duodenum with the T tube in the common duct projecting into the duodenum is of value in preventing obstruction of the duct while the inverted end of the duodenum is healing

part of that structure which is so much needed for safe inversion, or one may tear directly into the bile duct, a casualty in duct destruction which sometimes cannot be repaired satisfactorily. In such low ulcers adherent to the duct, mobilization of the duodenum below the point where the duct passes behind it and turning the duodenum inward and upward exposes the retroduodenal duct where it is not caught in the ulcer scar, and dissection of the duodenum upward from the exposed duct may be accomplished not only with protection of both these structures but often frees a surprising amount of duodenum proving valuable in the safe inversion of the duodenal stump (Fig 4).

To summarize our experiences with ulcers of this type, we advocate the insertion of a long-limbed T tube into the common duct and through the sphincter in the removal of

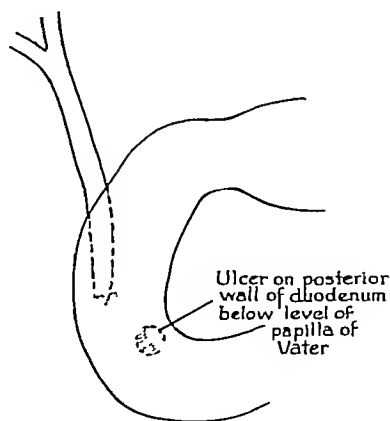


Fig 2 The location of the ulcer in 2 cases in which it was actually below the level of the point where the common duct entered the duodenum

certain low lying duodenal ulcers. There are certain gristly types of exudate in low duodenal ulcers involving the bile duct in which subtotal gastrectomy with removal of the ulcer is unsafe and contraindicated. The safest way to separate a low duodenal ulcer which has involved the common duct is by mobilizing the duodenum below the duct, thus approaching the duct outside the ulcer scar through an established retroduodenal line of cleavage.

The next problem which we wish to discuss is that of gastrojejunal ulcer following gastroenterostomy. Although its true incidence is unknown, it is high, perhaps over 15 per cent. It is more apt to occur in young people with high acids and is more intractable to nonoperative management than a primary ulcer in the duodenum or stomach. It can occur very early or very late after anastomosis of the stomach to the jejunum. We have had one occur 7 weeks after operation and several 15 to 20 and even 27 years after operation. However, we have successfully treated patients with gastrojejunal ulcer medically, and we have observed the healed scars of gastrojejunal ulcers in gastroenterostomy stomas at operation for other lesions. We believe the occasional spontaneous closure of a gastroenterostomy stoma is often due to the scarring secondary to a healing gastrojejunal ulcer.

We have performed 46 operations for gastrojejunal ulcer in patients who had had a

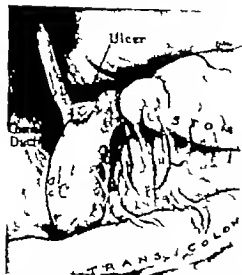


Fig. 3 It is difficult to illustrate cartilage in duodenal ulcer in drawing the common duct. The artist has ever has attempted to portray the difficulty. High could arise, in trying to separate such an ulcer and in of ed duodenum from the common duct.

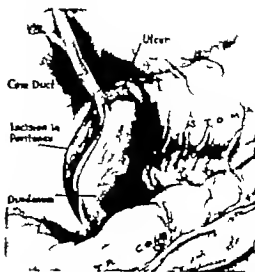


Fig. 4 Not the incision of the parietal peritoneum beside the duodenum, the duodenum rolled in, and the common duct mobilized. By this plan the common duct can be separated from the ulcer and it adherences much more readily than if approached from above.



Fig. 5 The arrow shows gastrojejunal ulcer already adherent to the transverse colon. Immediate surgery as and should be undertaken before it is possible for perforation into the transverse colon to take place, with the result that gastrojejunocolic fistula is created.

gastroenterostomy. There was 1 death. If there is any ulcer state in which the low gastric acids or anacidity so frequently occurring after high subtotal gastrectomy is essential it is in the cases of gastrojejunal ulcer. In this group high postoperative acidity which has a tendency to produce recurrent ulcer has usually been demonstrated. In such cases extremely radical and high subtotal gastrectomy is particularly necessary to produce postoperative anacidity or acidity below 10.

One type of gastrojejunal ulcer for which we believe immediate subtotal gastrectomy should be undertaken is the gastrojejunal ulcer adherent to the transverse colon (Fig. 5). This is the stage of gastrojejunal ulcer preceding erosion into the transverse colon and production of a gastrojejunocolic fistula, and in such cases operation should be undertaken before the ulcer perforates into the colon and produces a more dangerous and complicated technical problem. On operation in the case illustrated in Figure 5 the ulcer had already eroded through the muscularis but the mucosa was still intact permitting separation without perforation and contamination of the contents of the colon.

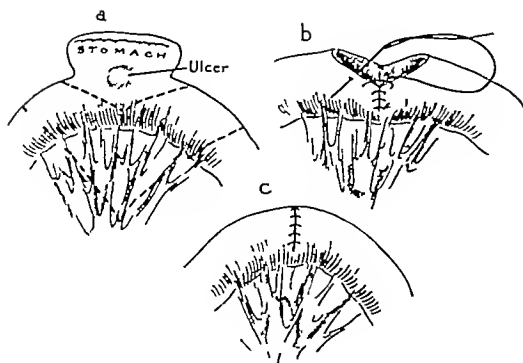


Fig 6 The method previously published (F H L) by which a gastrojejunal ulcer may be removed without completely transecting the jejunum. Note that closure of such an opening into the jejunum leaves the caliber greater than it was originally. Such a partial resection of the jejunum has less tendency to produce temporary obstruction and closure is simpler than with complete transection and complete end to end anastomosis.

Little need be said about the now quite standardized procedure of subtotal gastrectomy for this lesion except to call attention to two technical procedures which have proved valuable to us.

Sometime ago one of us (F H L) described a method of taking down a gastroenterostomy without completely cutting across the jejunum, thus requiring a complete end-to-end anastomosis (Fig 6). In this procedure only a fraction of the entire caliber of the jejunal wall is removed and the mesentery remains intact. This plan permits safe reunion of the bowel wall edges without dealing with the mesenteric border of the jejunum, and so re-establishes the caliber of the jejunum that it is larger than it was originally.

In separating the proximal and distal loops of a gastroenterostomy in subtotal gastrectomy for gastrojejunal ulcer, particularly of the so called no-loop variety, the proximal jejunal stump of the gastroenterostomy may be found to be very short. One of us (F H L) has described a method of transposing a short proximal jejunal stump under the vascular mesenteric root by incising the parietal peritoneum about the ligament of Treitz and closing the cut end of the proximal loop of jejunum, tucking it under the vascular mesenteric root, and bringing it out through the parietal peritoneum on the right side for an

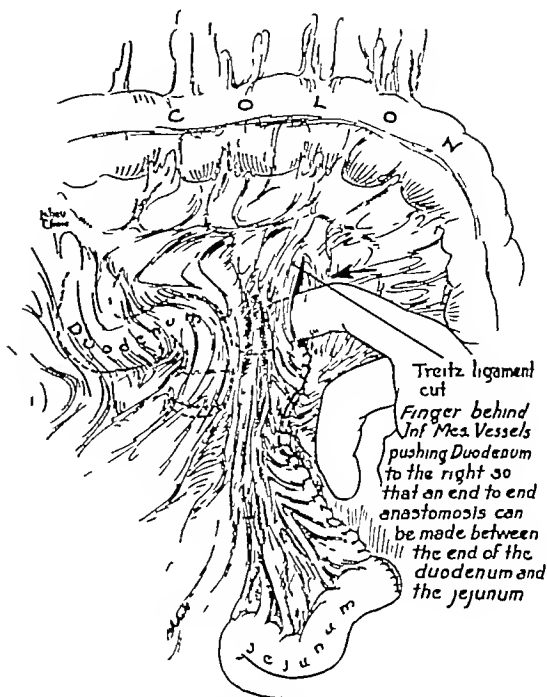


Fig 7 The parietal peritoneum has been cut about a short jejunal stump, the end of which has been inverted. The short stump has been pushed beneath the mesenteric vessels where it can be pulled through the right mesenteric peritoneum and anastomosed to the distal end of the jejunum by end to end or lateral anastomosis, as preferred.

anastomosis, or turning down the hepatic flexure for antecolic-duodenal-jejunal anastomosis. This has occasionally proved of great value in simplifying the management of gastrojejunal ulcer with a short proximal jejunal loop, and may be particularly valuable after resection of the right and transverse colon in gastrojejuno-colic fistula when the jejunal fossa and the short jejunal stump can be so well visualized (Fig 7).

A gastrojejuno-colic fistula is a most serious complication of gastrojejunal ulcer. It presents not only difficult technical problems in its surgical management, but particularly when the fistulous opening into the colon is large, occasions serious constitutional disturbances. Since much of the food in the stomach passes directly through the fistula from the stomach into the colon, weight loss and avitaminosis effects approaching those of pellagra occur. In addition, the escape of



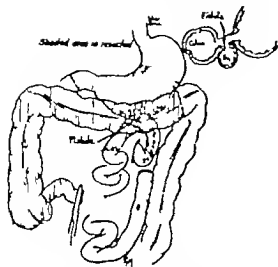


Fig. 8 The first step in the surgical management of gastrojejunocolic fistula. The ileum has been cut off close to the ileocecal valve, the proximal end turned in, and anastomosed laterally to the descending colon. The terminal distal segment of the ileum is to be turned in and dropped back into the abdomen until the second stage of the operation. Months later. The shaded area represents the block of colon, jejunum, stomach and duodenum to be removed intact at the second stage of the operation. By means of this plan the jejunal ulcer segment of jejunum involved, and its perforation into the transverse colon, is removed without making the transverse colon anastomosis without spilling any of the colon contents. The right upper corner is shown. Fistula connecting the stomach, jejunum and colon, indicating how desirable it is not to open the fistula but to close the colon.

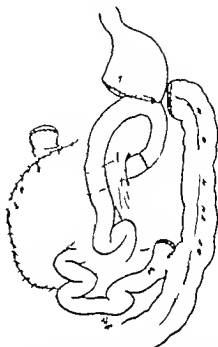


Fig. 9 The second stage operation for gastrojejunocolic fistula has been completed. The removal of the right half of the transverse colon, the ascending colon, the gastrojejunocolic fistula, and resection of the portions of the jejunum which is involved in the ulcer and the stomach. The ileum has been anastomosed to the descending colon as in the first stage of the procedure. This is to be carried out.

feces into the stomach and with this the belching of skatole has a most depressing effect on appetite. It is not surprising that severe degrees of inanition not infrequently accompany this complication and up to the time we developed the procedure illustrated here probably played a considerable part in fatalities. When the gastrojejunocolic fistula is small it can be satisfactorily managed by separation and closure. When it is large it is less possible to separate it safely and close the fistula into the colon without dangerous contamination of the peritoneal cavity. Because of this danger the procedure illustrated here was developed by one of us (F. H. L.) and has been used by both of us in a total of 8 cases. One death has occurred and that after the first stage.

As the first step in this two stage method of management of gastrojejunocolic fistula (Figs.

8 and 9) the ileum is divided a short distance from the ileocecal valve and the ends of the distal and proximal stumps of divided ileum are carefully inverted. The inverted distal end of the ileum is dropped back into the abdomen and the proximal ileum is anastomosed laterally high to the descending colon. In this way a good part of the fecal stream is directed into the colon beyond the point of the fistula into the stomach and jejunum. The patient is then sent home for two months, during which time in our experience he shows considerable general improvement together with a gain in weight.

At the second operation the ascending colon and short stump of the ileum are mobilized from their position on the posterior abdominal wall by including the lateral fold of peritoneum and ligating its mesentery. The blood supply

of the transverse colon up to and beyond the gastroenterostomy but proximal to the splenic flexure is ligated and these structures freed from their mesenteric attachments. The transverse colon well to the left of the fistula is closed with the De Petz sewing machine, cut across, and its ends safely inverted. With the transverse colon turned up, the proximal and distal loops of the jejunum leading to the gastroenterostomy are cut between clamps. The stomach is devascularized, the duodenum cut across and inverted, the sewing machine placed high up on the stomach and the structure cut across with the cautery between the double row of clips of the sewing machine. This permits lifting out of the field in one block all the colon up to the splenic flexure with the fistula in it unopened, the section of the jejunum anastomosed to the stomach at the point of the old gastroenterostomy with the gastrojejunal ulcer and fistula onto the colon, the lower two-thirds of the stomach with the gastroenterostomy, the gastrojejunal ulcer, and the fistula into the colon unopened and undisturbed. With this mass of intestine out of the way, the re-establishment of the jejunal canal by lateral or end-to-end anastomosis is much simplified since it is now so clearly visualized. If the resulting proximal jejunal stump is unduly short, it may be freed from the parietal peritoneum above the ligament of Treitz, as described above (Fig 7), pushed beneath the mesenteric root, and the anastomosis completed in front of the mesenteric root. With the anastomosis of the jejunum complete the typical Hofmeister anastomosis of the jejunum to the gastric stump may be completed in an open and unhampered field.

To those inexperienced with this type of gastric surgery, this may seem an operative undertaking of forbidding magnitude. Perhaps our experience with colonic, gastric, and jejunal resections causes us to minimize its magnitude, but we do not think so. We believe that the removal in one piece of the ascending colon, the right half of the transverse colon, and the jejunum and stomach, with the contained and unopened ulcer and fistula, not only adds to the safety of the operation from the point of view of contamina-

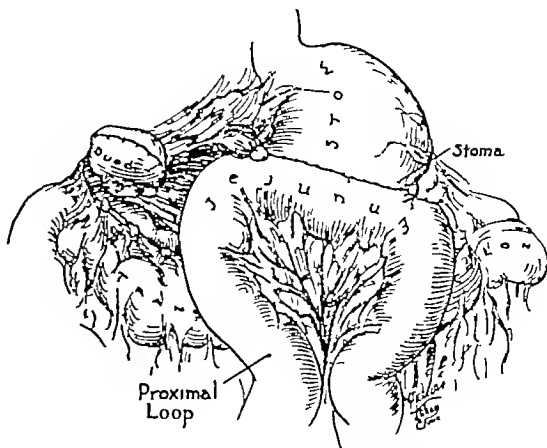


Fig 10 The long antecolic loops and the antecolic position of the gastric stump in antecolic anastomosis in subtotal gastrectomy for ulcer. This drawing shows the ease with which recurrent gastrojejunal ulcer after subtotal gastrectomy can be managed with this type of antecolic anastomosis. Note the antecolic position of the gastric stump just beneath the abdominal wall and the long loops of antecolic jejunum making easy further resection of the stomach and jejunal segment.

tion, but actually by providing better exposure and approach to the jejunum and stomach for re-establishment of the streams, adds to the ease and speed with which the operation can be done, particularly when the fecal stream has previously been established and is functioning beyond the level of that portion of the colon being dealt with.

In our surgical experience with the treatment of peptic ulcer in this series by means of subtotal gastrectomy, we have demonstrated in 5 cases gastrojejunal ulcer involving the jejunum at the anastomosis to the stump of the stomach. This is the fourth group to be considered. Every surgeon who has dealt with the problem of subtotal gastrectomy for ulcer must admit the possibility of a gastrojejunal ulcer even after this operation. With that in mind, we have repeatedly stressed the need for consideration of such a possibility when the subtotal gastrectomy is undertaken, and the need of so doing the operation that should a gastrojejunal ulcer occur it can be handled satisfactorily. For a number of years, in all subtotal gastrectomies we have employed antecolic anastomosis to the stump of the remaining stomach, without jejunojejunostomy.

This procedure has now been used in a sufficient number of cases without the production of obstruction and with satisfactory function so that we believe it not only has no disadvantages but many advantages (Fig. 10).

Its primary advantage concerns this fourth type of complicated ulcer problem, that is secondary resection of the stomach when gastrojejunal ulcer follows a high subtotal gastrectomy with which we have had to deal in the 5 cases. It is here with the antecolic anastomosis with long loops available in front of the transverse colon with the indurated gastrojejunal ulcer in the gastric stump free in the abdomen, and with the gastric stump accessible in front of the transverse colon that secondary resection after previous subtotal gastrectomy can most easily and safely be done (Fig. 10).

We present this method of anastomosis which we have now employed for many years not only for ulcer but also for cancer not as an argument against the continued use of posterior retrocolic anastomosis of the jejunum to the gastric stump after subtotal gastrectomy except on the basis that when gastrojejunal ulcer occurs in the posterior anastomosis, the exudate can well involve the root of the mesentery, of the transverse colon, the middle colic artery and may do so to the extent that it is impossible to preserve this vessel. Thus, in addition to subtotal gastrectomy with such a complication it has sometimes been necessary to do a resection of the transverse colon.

We personally wish to express our preference for the antecolic anastomosis without enterointerostomy because it provides a large amount of alkaline jejunal content in the long loop to be dumped into the stomach to help neutralize the gastric acidity and because it functions so satisfactorily without complications. We have had no obstruction or ballooning of the proximal loop. In only 2 cases, early in our experience before we dared to wait was reoperation done because of failure of the anastomosis to drain and in neither case was anything done because the obstruction was found to be due to edema and was relieved with no technical step whatever

applied to the anastomosis. In the large series of cases in which we have performed subtotal gastrectomy not only for ulcer but also for cancer and even in most of the 24 cases in which we have now done a total gastrectomy antecolic jejunal-gastric and antecolic jejunal esophageal anastomosis have been done without enterointerostomy and without complicating obstruction.

There is little to be said regarding the management of recurrent jejunal ulcer after subtotal gastrectomy except to call attention to the fact that in such a case a secondary subtotal gastrectomy is much easier and safer to perform when the anastomosis is of the antecolic type without lateral jejunojejunal anastomosis than when it is a retrocolic anastomosis.

#### SUMMARY

1 The surgical management of some of the more complicated peptic ulcers in the last 251 consecutive operative cases is discussed.

2 Of the 7,000 patients with ulcer whom we have hospitalized on medical management 18 per cent of the gastric ulcer patients and 6.50 per cent of the duodenal ulcer patients were submitted to operation.

3 A mortality rate of 2.7 per cent is reported in all gastric duodenal and gastrojejunal ulcers, exclusive of gastrojejunocolic fistula.

4 A mortality rate of 3.2 per cent is reported in 251 subtotal resections for ulcer of all types—gastric, duodenal gastrojejunal and including gastrojejunocolic fistula.

5 A mortality rate of 4.4 per cent is reported in 46 consecutive subtotal gastric resections performed solely for gastrojejunal ulcer.

6 Conservative operative methods are occasionally imperative to avoid high operative mortality in certain densely adherent duodenal ulcers or ulcers arising low in the duodenum and involving the common duct.

7 Radical subtotal gastrectomy is necessary for relief of the surgical gastrojejunal ulcer. Temporizing operative procedures in view of the possibility of recurrent ulcer serve only to increase further the operative risk.

# ONE STAGE COMBINED ABDOMINOPERINEAL RESECTION FOR MALIGNANT TUMORS OF THE RECTUM, RECTOSIGMOID, AND LOWER PART OF SIGMOID

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FOR some time it has been my opinion, which has been shared by others, that in the majority of cases of malignant growths of the rectum, rectosigmoid, and lower portion of the sigmoid, one stage combined abdominoperineal resection, when feasible, is the surgical procedure of choice, because it best satisfies the guiding principles of therapeutics for the pathological condition and for the patient.

This statement can be shown to be true for a particular surgeon only if a review of his cases demonstrates that such treatment was justified, and such justification is determined by the results obtained from the way in which he happened to deal with patients. If results are poor, it does not follow that he should discard one-stage combined abdominoperineal resection, but rather, perhaps, that the method of doing it should be discarded. If results are good, it also follows that they are never so good that they cannot be improved. It is, therefore, with the purpose of re-evaluation of my own opinion of one-stage combined abdominoperineal resection that this study is undertaken.

Without further elaboration, it is to be understood that my initiation and efforts in this particular surgical approach to the problem have been stimulated by the many excellent teachers and writers on this subject abroad and in this country.

The study is based on a consecutive and all-inclusive series of 276 cases in which I have performed the operation under discussion. In these 276 cases, counting deaths from all causes, regardless of the length of the hospital stay, 17 patients died.

There are many ways to break down any group of cases in an effort to arrive at answers

to questions which may be thought to be important. Too minute divisions, without sufficient numbers in any division, are likely to lead to the formation of false conclusions by the imputing of qualities or blame undeservedly to a method or to a detail of the therapeutic picture, therefore, no effort will be made in this article to intimate a supposed fact unless it is justified by a sufficient number of cases.

My experience with the one stage combined abdominoperineal resection reached a point at which I felt that I had accumulated enough cases to review them very critically, individually and as a group. At that time I had performed 105 such operations, with 15 postoperative deaths. As a result of the study, I was convinced that the mortality rate was too high, that if improvement was to be made, changes had to take place somewhere along the line, in preoperative preparation, in the surgical procedure itself (which includes anesthesia), and in the postoperative care. I had still another premise, and that was that each change must be simple and logical.

In the last 171 cases in which I performed one stage combined abdominoperineal resection for malignant growths of the rectum, rectosigmoid, and lower part of the sigmoid, there were 2 postoperative deaths. One death was caused by peritonitis which resulted from an abscess that developed just above the sacral promontory and ruptured intraperitoneally on the 12th day after operation, the lesion in this case was a lymphosarcoma, grade 4, of the rectum. The other death, also in a man, occurred on the 9th postoperative day as a result of sudden and massive pulmonary embolism. This man weighed 235 pounds (106 kg) and was operated on for a grade 1 (type A, according to Dukes' classification) lesion of the rectum.

From the Division of Surgery, Mayo Clinic.  
Read before the meeting of the Inter State Post Graduate  
Medical Association, Chicago, Illinois, October 26 to 30, 1942.

The abrupt and up to this time lasting improvement in the surgical mortality rate is another justification for the present report. It is my intention to consider herein those measures in the preoperative preparation, anesthesia, the operation and the postoperative care which have had a major part in the improved results obtained.

#### PREOPERATIVE PREPARATION

Let me now consider points in the preoperative preparation.

First, the patient is admitted to the hospital for preparation at least 48 hours before operation.

Second, any patient who has a malignant tumor in the anus, rectum, rectosigmoid, or lower part of the sigmoid for whom there is the remote possibility of performance of a one stage combined abdominoperineal resection is prepared preoperatively for it (that is, the fact that a growth feels firmly fixed on examination from below does not justify the assumption that it will not be possible to perform the operation after surgical exploration from above) It is assumed that the patient has been properly shaved and has come to the operating table with an indwelling urethral catheter accurately in place. Thus will be avoided unnecessary delay on the operating table or perhaps, a second choice type of operative procedure.

Third measures for the emptying and cleansing of the colon may vary depending on the degree of obstruction present and unfortunately on the question of whether or not barium has been given by mouth. Although few patients will require any preliminary measure such as cecostomy if obstruction is marked the case usually is not one in which the one-stage operation should be selected. Unless the bowel is well emptied such a major surgical procedure as that under discussion should not be attempted. A well prepared bowel is an essential if a low mortality rate is to be maintained for this operation. Use of a high carbohydrate nonresidue diet the taking of laxative agents by mouth (I use phosphosoda) and irrigations administered from below with the patient in the knee-chest position, repeated as indicated will

suffice to empty and sufficiently cleanse the colon in most instances.

Fourth, if debility dehydration anemia or other complicating features exist and can be rectified within a comparatively short time to such a degree that a major surgical procedure is not contraindicated, they should not in themselves, prevent the operation. Evaluation as to the patient's reserve powers against the shock of a major operation is to be made in all cases, and possible complications are to be anticipated by the use of preoperative measures.

Fifth, mental preparation is, I believe important. When a surgeon plans a one stage combined abdominoperineal resection, he is not always able to complete the plan after surgical exploration has been carried out therefore it is important for him not to commit himself beforehand. Most patients will know or at least, have a good idea, of what their trouble is, before operation. Mental preparation should for the most part evolve from mental adjustment to the possible performance of colostomy. The surgeon should beware of a patient who is sure before operation that death will ensue.

Sixth antiperitonitis vaccine in doses of 1 to 1.5 cubic centimeters, is injected with a dull pointed needle intraperitoneally, in the right lower abdominal quadrant 48 hours before operation. It is my opinion that this is a therapeutic adjunct not a panacea and although I cannot accurately evaluate its usefulness at least I have never had experience with it in any case in which I could see it was harmful and indications are that deaths from peritonitis are fewer in those cases of lesions of the colon in which it has been employed than in those in which it has not been used.

#### ANESTHESIA

Next the subject of anesthesia can be discussed appropriately. The type of anesthesia which has been used in the vast majority of cases on my service for this operation has been a combination of spinal anesthesia—with procaine hydrochloride or benzyl-gamma-(3 methylpiperidino)-propanol hydrochloride (metycaine)—and intravenous anesthesia with pentothal sodium. There have been a few

exceptions to this procedure, as determined by the judgment of the anesthetist. This follows the axiomatic statement that the anesthetic agent to use in any case is that with which the anesthetist is most familiar and which is best suited to the individual case.

In my opinion, timing of the combining of spinal and intravenous anesthesia is important. One should not delay use of any combination type of anesthesia until the effect of the first type used gives evidence of wearing off. We anesthetize the patient by the intravenous technique, approximately at the time the abdominal incision is made and continue this form of anesthesia until the posterior resection has been completed.

The dosage of the spinal anesthetic agent is the same as that which would be used were combined anesthesia not contemplated. The dosage of pentothal sodium will vary, depending on the response of the individual patient to it. Oxygen of a high concentration also can be administered by the inhalation mask, with apparent benefit.

A more detailed discussion of the subject of combined spinal and intravenous anesthesia for operations on the colon has been published elsewhere.

Additional supportive measures may be indicated during the course of the actual operation, such as those required because of an unusual decrease or increase in the patient's blood pressure or an unusual loss of blood; these measures should be thought of as something to be carried out immediately, and not after operation. Frequently, solutions of sodium chloride or of glucose are administered intravenously and, more occasionally, blood is transfused at the time the patient is on the operating table.

#### OPERATIVE METHOD

An essential of the carrying out of any operative method is a thorough understanding on the part of the surgical team of the details of that method, from the time the patient is placed on the operating table until he is moved off. This will avoid unnecessary and even hazardous motions and loss of valuable time and make for the efficiency and pleasure of all concerned.

I have no quarrel with the surgeon who prefers other types of instruments or suture material than those which I use. A difference of opinion might be based on how the instruments and suture material were used, rather than on the instruments and materials themselves.

What will be presented here is a description of a method of one stage combined abdominoperineal resection which has given good results.

*The incision.* A low abdominal incision is made approximately 1 inch (2.5 cm) from the midline, through the anterior fascia of the left rectus muscle, and the muscle is retracted laterally. This incision is selected because it interferes the least with the blood and nerve supply to that muscle, and experience has proved that it is a good one through which to work in order to complete the operation in one stage, to set the stage for a two stage combined abdominoperineal resection, to create a permanent type of colonic stoma, or to close as only an exploratory operation.

*Exploration.* The purpose of examination of the abdominal cavity is to determine the feasibility and justifiability of the operation in one stage. Gross evidence of distant metastases, particularly in the lobes of the liver, is felt for; the abdominal portion of colon should be palpated carefully, with the realization that in 5 per cent of cases of malignant processes of the colon the condition is multiple; fixation of the lesion itself is estimated. The combination of observations determines the question as to whether or not one stage combined abdominoperineal resection should be attempted. There are, of course, all degrees of indications in the observations and, as time goes on and experience accumulates, the surgeon is tempted to assume greater and greater risks. A small degree of metastasis to the liver with a primary movable lesion of the rectosigmoid, for instance, would not necessarily contraindicate the operation, nor would obesity itself or a movable, additional, small, nonobstructing lesion in the transverse colon or splenic flexure contraindicate it.

*Operation proper.* If the decision is made to proceed with the surgical maneuver planned on, the incision is enlarged to an adequate size.

It is a mistake to work through too small an incision. Dr. William J. Mayo used to say that it was well to remember that an incision heals from side to side, not from end to end.

The next step is to examine the sigmoid carefully principally so that it can be decided at which point colostomy should be performed. This depends on the mobility of the colon and mainly on how much, if any, redundancy exists. Colostomy is not to be standardized; a point in the incision will be found where the portion of bowel to be exteriorized will come out the easiest and it should be so planned that if possible about 3 inches (about 8 cm.) of colon will protrude beyond the margin of the skin. Also this point in the bowel should be so selected that there will be very little redundant bowel proximal to the colonic stoma, so that prolapse at a later time will be avoided.

When the site in the sigmoid colon has been selected for colostomy a rubber tube is run through the mesosigmoid next to the bowel and then, with the patient in the Trendelenburg position, the small intestine is packed away from the region of dissection.

Dissection of the lower segment of colon is begun just below the rubber tube which has been placed at the point selected for colostomy. The peritoneal covering of the mesosigmoid is peeled back, so that the branches of the sigmoidal vessels are exposed; these branches are ligated. This procedure is continued until clamps can be applied high on the superior hemorrhoidal artery. Usually the site for application of the clamps will be 3 to 4 inches (about 8 to 10 cm.) above the promontory of the sacrum. Looking forward to the stage in the procedure at which the pelvic peritoneum must be closed it is important to preserve as much healthy peritoneum as possible during these first steps. The right ureter is very easily avoided; the left, particularly in obese patients, must be more carefully protected because the left position of the mesosigmoid makes it more vulnerable than the right one.

Up to this point the dissection has been carried out above the rectum, posteriorly and bilaterally. If rectal dissection is next carried out posteriorly to the tip of the coccyx and

laterally, approaching anteriorly as well as is possible in the individual case, anterior dissection will be more easily accomplished because of the increased mobility. Long scissors will be a distinct advantage. The lines of cleavage of the fascial planes should be followed and the surgeon should keep ever before him the objective which is to stay well away from the involved tissues. Each case will be different in respect to the ease of this part of the dissection. Effort should be made to accomplish as much of the rectal dissection from above as possible; for this technique will facilitate the work posteriorly. When as much as can be done has been done the surgeon should not keep trying to do more.

Next attention is directed toward placement of the colonic stoma. Again the proximal portion of sigmoid is pulled up and the point in the incision through which the bowel will pass most naturally is marked. Here the subcutaneous fat is pushed laterally from the anterior rectus fascia, muscle from the under surface and muscle from the anterior surface are separated laterally from the posterior fascia; the anterior and posterior fascia are then cut transversely and the left rectus muscle is separated with curved forceps in such a manner as to leave about 1 inch (2.5 cm.) of muscle on the normal side. The fascia is cut thus in order not to strangle that portion of bowel which is to form the colonic stoma.

Long Payr clamps are slid through the split in the left rectus muscle and are applied at the desired point on the sigmoid. A smaller Payr clamp is placed on the lower part of the sigmoid, the bowel having been elevated in such a manner as to allow removal of any redundant portion. It is important to leave no more bowel to be placed in the dissected rectal space of the sacrum than necessary.

The next step is to close the distal stump of sigmoid. Closure is accomplished by an over-and-over suture across the closed Payr clamps. By withdrawal of the clamp as the suture is pulled the crushed portion is inverted. The lower segment of colon is now placed deep under the pelvic floor and the peritoneal edges are brought together with double strands of No. 1 chromic catgut and, beginning at the base of the bladder in the male and at the base

of the uterus in the female (if she has not been divested of this organ), this suture is continued to the point at which the mesentery of the sigmoid is to penetrate the posterior rectus fascia and there it is locked

At this stage decision is made for or against closure of the lateral space between the site of colostomy and the abdominal wall. The rule which I follow is (1) close small openings and leave large ones open and (2) close nothing under tension. Actually, I will close only a small percentage of openings. Having either closed or left the aforementioned space open, I now continue, with the suture with which the new pelvic floor has been approximated, to close that portion of the abdominal incision lying below the colonic stoma.

The abdominal pack is removed next and the patient is moved from the Trendelenburg position into the horizontal position, and the upper portion of the abdominal incision is closed. Care is taken not to close incision too tightly around colonic stoma, a finger should slip in easily between bowel and fascia.

After closure of the skin has been carried out, a fishline pursestring suture is placed just below the Payr clamp on the single barrel colonic stoma, the clamp is removed and a rectal tube is placed about a half inch (about 1 cm) into the lumen of the bowel, where it is fixed in place. It is most important to be certain that the tube does not extend below the margins of the skin. Edema and swelling may sever the bowel between the fascia and the rubber tube, should the tube be allowed to go in too far.

The anterior wound is then dressed so as to avoid pressure on the extruding colonic stoma and the patient is placed carefully in the lithotomy position. The buttocks and anus are cleansed and a pursestring suture of the fishline is placed about the anus to prevent leakage. A triangular incision next is made, the base being up and the apex being at the tip of the coccyx. The size of the triangle will depend on the situation of the malignant lesion, for those situated high it need not be as extensive as for those situated low. The coccyx need not be removed. I have never removed it in this operation and I know of no case in which it had to be removed later on.

If dissection has been carried out, as would be preferred, from above, posterior resection is comparatively simple, infrequently requiring more than from 10 to 15 minutes for completion. Bleeding points are caught and ligated, and after the posterior cavity has been swabbed with tincture of sodium ethylmercurithiosalicylate (merthiolate) and 75 grains (4.9 gm) of sulfanilamide crystals have been placed in it, a rubber composition sheet (pliofilm) is placed over the opening and a long gauze strip is packed snugly into the cavity for a twofold purpose (1) to control bleeding and (2) to support the new pelvic floor against immediate stress and strain.

The posterior pack is left in place for 4 days and the single stitch that has kept it in place is then removed and the pack is gently pulled out, care being taken that it does not create suction by being removed like a cork. Very little, if any, sedation is required for removal of the posterior pack.

#### POSTOPERATIVE CARE

Postoperative care can be divided roughly into two important divisions (1) general supportive measures and (2) local care of the wounds. It is understood without elaboration that competent nurses must have a thorough understanding of the nature of the operation and of the details of carrying out postoperative orders, for in their heads and hands much of the responsibility lies.

*General measures.* Transfusion of blood. All patients, regardless of how well they may have tolerated the actual surgical procedure, receive 500 cubic centimeters of whole blood by transfusion. If there is any question as to whether more blood is needed, the element of doubt alone is taken as an indication that it is, and then 1,000, instead of 500, cubic centimeters of blood is transfused. It is well to state here that before operation, in anticipation of the need for transfusion, the blood of the patient should be typed, as should also that of the relatives, as potential donors.

*Oxygen.* All patients receive postoperatively high concentrations of oxygen, either in the oxygen tent, where the concentration is kept in the vicinity of 50 per cent, or by means of the B L B mask (nasal or oronasal, as indi-



cated) in which the concentration approaches 100 per cent. The minimal duration of administration is 24 hours, but oxygen can be given for longer periods, if it is indicated.

**Activity** At the clinic we like to keep our patients moving in bed and to have them up and out of bed at the earliest opportunity. The magnitude of the operation is too likely to be assumed to be an indication for prolonged rest in bed. Unless it is contraindicated, however and it rarely is, our patients "dangle" (swing the feet off the side of the bed and remain in a sitting position for a short time) morning and afternoon of the 9th postoperative day and get out of bed on the 10th day at which time daily sitz baths are begun. Between 80 and 85 per cent of patients can be up and out of the hospital in less than 3 weeks after the operation. They should not be permitted to make invalids of themselves.

**Mental attitude** It is the obligation of the physicians and nurses in attendance to aid by every means possible in the adjustment of the patient to the acceptance of a permanent colonic stoma. The patient's natural tendency is to think only of the bad features of a colonic stoma and the probable limitations in habits of living which will ensue.

**Care of the abdominal and posterior wounds**  
**Abdominal wound** Strict adherence to certain principles will have much to do with what may be termed a "good" abdominal wound. First, it should be kept unsoiled by fecal material for as long as possible. The rectal tube tied in the lumen of the colonic stoma, as previously described aids in this. Second, when soiling finally becomes unavoidable fecal material must not be allowed to remain in contact with the wound. Close attention by a nurse is a requisite and frequent exposure of the wound under a cradle with or without the application of dry heat is mandatory. Third, undue pressure must not be exerted on the colonic stoma. It should be dressed with a doughnut type of dressing, about the protruding portion of bowel.

**Posterior wound** The posterior wound is left practically undisturbed until the 4th post-

operative day at which time the pack is removed. Our efforts are bent toward keeping the outer part of the wound wide open by daily examination with the sterile gloved finger so as to avoid pocketing deep in the wound. Slight "spilling" of the temperature postoperatively from about the 8th day on frequently will be caused by walled off pockets in the posterior wound.

Cleanliness and stimulation of clear granulation tissue are achieved by irrigation, twice daily with an 0.5 per cent solution of sulfanilamide alternating with a quarter strength solution of hydrogen peroxide and also by daily sitz baths from the 10th day on, when the patient is out of bed. The vast majority of these patients can sit with surprising comfort from this time on and by the 6th week the posterior wound generally is well on toward complete healing.

The sum and substance of dealing with the posterior wound is to allow it to heal cleanly from within outward.

#### CONCLUSION

Although I have spoken generally of a series in which one stage combined abdominoperineal resection has been performed 276 consecutive times on my surgical service up to October 3, 1942 and in which there were 17 postoperative deaths or a mortality rate of 6.15 per cent my main attention has been given to analysis of the preoperative care, the surgical details, and the postoperative attention in the last 171 cases in which 2 deaths have occurred (counting all postoperative deaths from any cause regardless of the time the patient spent in the hospital) resulting in a mortality rate of 1.17 per cent.

The purpose of the study has been to present those factors in the care of these patients which I feel have had a major rôle in bringing about the improvement in this latter series of one stage combined abdominoperineal resection.

#### REFERENCES

1. ANDERSON, R. M., MORTON, L. H. and MARR, C. W.  
*Surg. Gyn. Obst.* 84:2, 75-85-67

# THE EFFECT OF HEPARIN ON WOUND HEALING

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THE anticoagulant action of heparin has made this substance a valuable adjunct in the prevention and treatment of thrombosis. Recent experiments indicate that heparin might inhibit the formation of intraperitoneal and intrapleural adhesions. If this be true, it raises the question as to what effect heparin might have upon the healing properties of a surgically induced wound. It is this question which we undertook to answer in our experiments.

*The indications and limitations for the use of heparin are not as yet well defined despite much excellent clinical work on the subject. This is probably due to the fact that its mode of action is not completely understood. It is hoped that our experiments might shed some light on this problem.*

Occasional cases of wound dehiscence following the postoperative use of heparin have been called to our attention. However, because of certain extraneous factors influencing the efficiency of wound healing in these cases, we were not convinced that heparin was the cause of wound disruption. It seemed proper, therefore, that a controlled study of the problem be undertaken.

Mason has shown that heparin apparently does not inhibit the healing of incisions in blood vessels. Bendix has studied the effect of heparin on the healing of gastric incisions in rats, using a compressed air distention technique. He found no appreciable effect on the 5th postoperative day.

## METHOD

In our experiments some 80 mongrel dogs of about the same weight were used. Under nembutal anesthesia and the usual aseptic precautions an incision exactly 3 inches long was made in the upper midline of the dog's abdominal wall. The umbilical area was not

incised. The incision was made through the linea alba so that no muscle was cut or separated. The peritoneum, which is adherent to the endoabdominal fascia in the dog's abdominal midline, was opened with the other mural structures.

The method of closure was identical in each animal. It consisted of placing 7 interrupted sutures of the No. 00 chromic catgut<sup>1</sup> to approximate the wound, each suture including all the mural structures. All bleeding points were carefully clamped and ligated with fine silk. The skin was closed with a fine subcuticular suture of fine silk.

Two series of dogs were followed. One series received multiple intravenous injections of heparin<sup>2</sup> so that the coagulation was at all times kept above normal, ranging from 5 to 120 minutes. In the control series the same operation was carried out but the animals received no heparin. At the time of wound disruption, blood protein and blood vitamin C determinations were made in order to rule out a deficiency of these factors as a cause of poor handling.

Groups of animals in each series were subjected to a wound disruption test at intervals between 1 and 22 days after operation. Daily tests were carried out between the 1st and 8th postoperative days. Because of the large number of animals used in the experiments we were desirous of finding a means of testing wound strength which would not necessitate the removal of a section of abdominal wall and the sacrifice of otherwise healthy dogs. We therefore devised a method which, though not quantitatively accurate, gave a qualitative or comparative determination of the amount of force necessary to disrupt the wounds. A specially designed instrument was built which

<sup>1</sup>Ethicon chromic (J & J). No. 00 meets the requirements stipulated in the U. S. Pharmacopoeia XI, 2d supplement being 5 pounds minimum average tensile strength on the straight pull and 3 pounds minimum average over the surgeon's knot.

<sup>2</sup>Liquemine (Roche-Organon, Inc.).

TABLE I — TENSILE STRENGTH OF A STANDARD TYPE OF ABDOMINAL WOUND IN THE DOG

Normal animals			Heparinized animals		
Age of wound in days	Force, in pounds, necessary to disrupt wound	Average	Age of wound in days	Force in pounds, necessary to disrupt wound	Average
	35	40		34	36
	35			33	
	40			36	
	33			30	
	34			5	
	45	40		30	36
	35			30	
	35			30	
	30	30		30	36
	30			30	
	30			30	
	35	30		30	36
	30			35	
	30			35	
1	30	30		35	36
	40			35	
	30			35	
6	35	37	6	30	30
	35			30	
	45			30	
	35	37		30	30
	35			35	
	35			30	
8	40	37	6	Normal tissue kept at 37° C. by the work wound still healed	
12	Wound withstood 200 lbs. tension			30	
12	Wound withstood by the tension through normal structure				

(Fig. 1) The retractor hooks were inserted into small puncture wounds placed  $\frac{1}{4}$  inch on either side of the middle of the incision. These wounds penetrated the entire thickness of the abdominal wall. By turning a crank mounted on threads, the retractor hooks were gradually separated. The maximal reading on the scale before actual disruption of a part or all of the mural structures (not skin) was taken as the force in pounds necessary to disrupt the wound.

We were aware of the fact that certain tangential forces were dissipated above and below the puncture wounds. However repeated determinations convinced us that these factors could be considered as more or less constant and could be disregarded as a source of error in purely qualitative determinations.

After the strength of the wound was tested the puncture holes and the ruptured incision were sutured thus allowing the animals to survive for use in other experimental work.

#### RESULTS

The tension force representing the degree of disruptibility in our control animals gave a fair index of the healing powers of a surgically induced abdominal wound in the dog when the blood protein and blood vitamin C levels are within normal limits (Table I).

In the control series, the wound was found to be weakest on the 4th and 5th postoperative days. The average disruption force in pounds for these days was 31 and 35 respectively. In the heparinized series, the wound was weakest on the 3d postoperative day at which time the disruption forces averaged only 14 pounds. It was found that beyond the 5th postoperative day the wound in both the heparinized and control series followed some what similar strength curves, so that it was concluded that heparin had no effect on the healing powers of an abdominal wall incision beyond the 5th postoperative day.

The only remarkable variance from the consistent results were instances in which there was found to be an abnormal amount of blood accumulated in the intramural tissues. It is well known that an excess amount of blood within the region of a healing wound will retard the progress of healing. It was

consisted of two opposing retractor hooks mounted on a metal rod. One hook was stationary while the other was attached to a sliding flange. The flange in turn was attached to a spring scale graduated in pounds

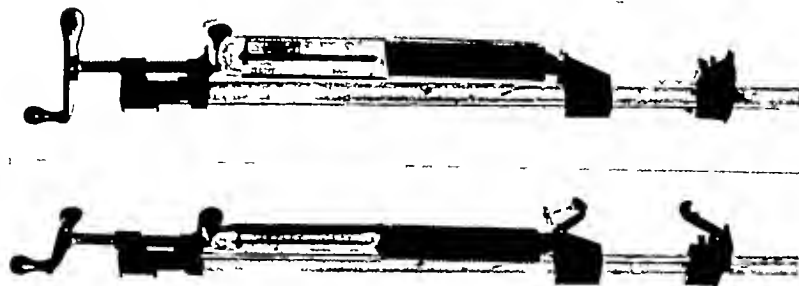


Fig 1 Two views of wound disruptor used in testing tensile strength of abdominal wound in the intact animal

assumed, therefore, that in such cases the hemostasis was not adequate enough to prevent the pooling of harmful amounts of blood in the healing wound after the administration of heparin. Those instances in which hemostasis proved adequate showed no remarkable difference between the heparinized and controlled series beyond the 5th postoperative day.

Laufman has shown that bleeding may resume after the administration of heparin, despite grossly satisfactory hemostasis at time of operation. There were several instances in each series in which the skin portion of the wound was found disrupted after the 3d postoperative day, with the mural portion nevertheless healing satisfactorily. Such skin disruption occurred spontaneously in 6 of the heparinized animals and in only 1 of the control animals. The potential space between fascia and skin, consisting of loosely packed subcutaneous fat makes an ideal pocket for hematoma formation. In no instance in either series was there spontaneous disruption of all of the structures of the abdominal wall.

Although our tests began with the 1st postoperative day, it soon became apparent that the tests were not of great significance until at least the 3d postoperative day, because of the holding power of the catgut. The fact that the heparinized animals had a comparatively weak wound on the 3d postoperative day when compared with the control series, made us wonder whether the catgut actually dissolved more rapidly in the presence of heparin. Isolated *in vitro* experiments, however, subsequently showed this to be untrue. Heparin did not hasten the dissolution of catgut.

Microscopic sections of wounds representing various stages of healing in control and heparinized animals were stained with Weigert's gram method<sup>1</sup> for fibrin. Up to and including the 3d postoperative day the wounds of heparinized animals were found to contain somewhat less fibrin than did the wounds of control animals. By the 4th and 5th postoperative days, however, the wounds of both the heparinized and control animals appeared to contain about the same amount of the bridging substance. It became apparent, therefore, that although heparin delayed the laying down of fibrin, it did not altogether prevent the process. By the 4th or 5th postoperative day the deposition of fibrin in the wound of heparinized animals apparently "caught up" to that in the control, despite a delay for the first 3 days. The growth of fibroblasts was altogether unaffected by heparin.

#### OBSERVATIONS

The exact mode of action of heparin is still controversial. There is, however, some agreement that it acts both as an antithrombin and an antiprothrombin. From all the available evidence, D'Alessandro concluded that heparin (activated by plasma) and thrombokinase are antagonistic, and that one promotes and the other inhibits the conversion of prothrombin to thrombin. Within certain limits of concentration, an excess of either counteracts the effect of the other. If this premise be accepted, heparin indirectly inhibits the formation of fibrin from fibrinogen. However, our experiments indicate that although the

<sup>1</sup>Using crystal violet and Lugol's solution and clearing in alcohol

coagulation time of the blood is prolonged by heparin such prolongation does not necessarily prevent but merely delays the deposition of extravascular fibrin.

#### CONCLUSION

In experimental studies on dogs, it was found that heparin had no appreciable effect upon the healing process of surgically produced abdominal wounds in dogs whose blood protein and blood vitamin C levels were within normal limits. The only deleterious action exerted by heparin upon the healing powers of a wound was the pooling of blood within the wound. This accumulation of blood in the presence of heparinization was apparently due either to inadequate hemostasis at the time of operation, or the resumption

of bleeding in the wound after apparently adequate hemostasis at time of operation. Heparin appeared to delay the healing process slightly up to the 4th postoperative day but after that it had no real effect.

We again emphasize as have other that when it is necessary to administer heparin after operation, the most meticulous hemostatic precautions be taken at time of operation. Whenever possible nonabsorbable or slowly absorbable suture material should be used.

#### REFERENCES

1. BRIDGES, R. Personal communication. Unpublished results.
2. D'ARNAUD, A. J. *Surg. Gyn. Obst. (Internat. Abstr. Surg.)* 94: 74, 62.
3. LUTCH, A. H. *Surg. Gyn. Obst.* 94: 74, 473.
4. MASON. Quoted by D'Arnaud. Loc. cit.

# THE USE OF VENOGRAMS FOR THE LOCALIZATION AND STUDY OF ARTERIOVENOUS FISTULA

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**V**ENOGRAPHY has become a well established procedure. The ease and safety with which it can be carried out makes it of material value in both the diagnosis and localization of lesions of the veins of the extremities. Its use has been confined principally to the study of venous thrombosis, and excellent treatises on this aspect, as well as detailed accounts of the technique, have been provided by Dougherty and Homans, and by Bauer. Bauer suggested that it might also be of value in the study of arteriovenous fistulas, although he had had no opportunity to verify this impression.

Traumatic arteriovenous fistula produces profound changes in the circulatory system, and while these changes involve both the arterial and venous sides, the latter is the more adversely affected of the two and is responsible for most of the signs and symptoms which characterize the disease. The changes in the vein consist of hypertrophy and dilatation, and vary in degree according to the caliber of the vessels involved, the size of the fistula, and its duration. The dilatation may be diffuse and may extend for some distance proximal to the level of the fistula, or may be maximal locally at the site of the fistula, where it represents an almost constant finding.

The venous trunk distal to the fistula does not exhibit the degree of dilatation seen proximally. Callander has called attention to the fact that as long as the valves remain competent, no changes are apt to occur, the increased venous pressure at the level of the fistula merely obstructing the passage of blood from below by imposing an obstacle against it. Should the valves yield or become insuffi-

cient due to the increasing dilatation of the vein above them, the adjacent distal segment then undergoes the same changes that are seen above, and Holman reports such an instance in which there was a large saccular dilatation just distal to an arteriovenous fistula of the superficial femoral vessels. Such dilatation is apparently uncommon, for the arterial blood, taking the course of least resistance, passes through the fistula and into the proximal vein. The essentially normal status of the involved vein distal to the level of the fistula makes it readily adaptable for venography.

Within a period of a few months, 3 patients with arteriovenous fistulas of the common femoral vessels were admitted on the surgical service of one of us (J.R.W.). Venograms, made in each of these prior to operation, permitted us to make certain observations which we consider worth reporting. These cases are reported only in sufficient detail to correlate the findings of the venograms.

**CASE 1** Willie Harrison, a colored male 49 years of age, was admitted to the Passavant Hospital in January, 1942, for treatment of an arteriovenous fistula of the right femoral vessels and a mass in the right lower abdominal quadrant. He had been shot in the posterolateral aspect of the right thigh 18 years before, when the bullet traversed the thigh and lodged just beneath the skin about 3 inches below the medial aspect of Poupart's ligament.

The positive findings on physical examination were limited entirely to the cardiovascular system. The heart was enlarged in all directions, with the maximal apex impulse in the 6th left intercostal space in the anterior axillary line. There was a systolic murmur which was best heard over the apex and which was transmitted to the left axilla and the right sternal border. A teleroentgenogram showed the transverse diameters of the chest and heart to measure 30.5 and 20.3 centimeters, respectively. There was a large mass in the right lower abdominal quadrant which measured 14 by 10 by 7 centimeters, and which appeared to occupy most of the quadrant.

From the Passavant and Presbyterian Hospitals and the John C. Oliver Memorial Research Fund of the St. Margaret's Memorial Hospital, Pittsburgh.



Fig. 1. Normal venogram Case 3, showing femoral and iliac veins, and also long saphenous vein at its junction with femoral vein. This venogram is inserted for comparison with the other venograms. The dense shadow overlying the external iliac vein is bullet.



Fig. 2. Venogram Case 3 showing the shadow of normal femoral vein up to the level of the head of the femoral bullet point it stops abruptly. There are numerous dilated and tortuous veins present in the soft tissues of the thigh.

The right leg was much larger than the left, there being 5 centimeters difference in circumference at the mid thigh and 7 centimeters at the mid-calf. There were varicosities and pigmentation, and in the region of the ankle there were two scars of healed varicose ulcers. There was constant thrill and bruit over the right groin just below Poupard ligament, the bruit being transmitted to the abdominal mass. The popliteal and dorsalis pedis vessels were not palpable.

A venogram (Figs. 1 and 2) was made of the right leg by injecting 50 cubic centimeters of 30 per cent diodrast solution into vein posterior to the inner malleolus. The femoral vein appeared to be normal and visualized just the level of the head of the femur here it stopped abruptly. There were numerous dilated and tortuous veins in the soft tissues of the thigh.

Operation consisted of quadruple ligation of the common femoral artery and vein, and obliteration of the fistula by suture. The fistula was found to be about 5 centimeters below Poupard ligament (Fig. 3). The artery and vein below the fistula were each

proximally 4 centimeters in diameter although measurement of the vein was inaccurate as part of it lay beneath the artery. There was some sclerosis of the artery. The wall of the vein was thickened, although it was not as thick as that of the artery. The vessels below the level of the fistula were small, the artery measuring centimeter in diameter while the vein was even smaller. There were several large arterial and venous branches entering the fistula, for the most part on its posterior aspect.

CASE. William Moctow, bit male 56 years of age, was admitted to the Presbyterian Hospital on January 24, 1921, for treatment of arteriovenous fistula of the left femoral vessel. He had been injured 8 years before when, while on the cab of an electric engine he was operating, exploded during fragment of glass into the groin.

On physical examination the patient found to be lying propped up in bed in obvious cardiac failure. He was dyspneic and slightly cyanotic. The left half of the chest was heaving forceful with each heart beat the impulses being visible over the carotid vessel. The superficial veins over the neck and

thorax were prominent when he was lying down but tended to disappear when he sat up. The apex impulse of the heart was maximal in the 7th left intercostal space at the anterior axillary line. There was a harsh blowing systolic murmur over the apex and aortic areas. Auricular fibrillation was present with a pulse deficit at the wrist. The blood pressure was 150 millimeters of mercury systolic and 50 millimeters diastolic. A teleoroentgenogram showed the chest and heart to measure 28.8 and 20.1 centimeters, respectively, in their transverse diameters. There were fine moist crackling râles throughout the lung fields, being most marked over the bases posteriorly. Examination of the abdomen revealed forceful pulsation of the aorta which was transmitted to the anterior abdominal wall. The liver was enlarged, extending four fingerbreadths below the costal margin. The left leg was larger than the right, with a thrill and bruit, and a visible heaving pulsation over the femoral triangle. The superficial veins were dilated and there was some pigmentation of the skin over the lower leg.

Venography (Fig 4) was effective in localizing the fistula, a normal femoral vein being visualized to the level of the lesser trochanter where it stopped abruptly. Some of the dilated superficial veins were also visualized.

Operation consisted of quadruple ligation of the common femoral artery and vein, and excision of the segment containing the fistula. The fistula (Fig 5) was found to be embedded in a mass of fibrous tissue and lay just above the point of origin of the profunda femoris artery. The artery above the fistula was found to be uniformly enlarged and was sclerotic. The vein was about twice the size of the artery, and above Poupart's ligament gave the appearance of being sacculally dilated. There were several large arteries and veins which communicated with the common femoral vessels above the level of the fistula and which passed over toward the pubis. There were also several other vessels which came up from the deep aspects of the thigh and communicated with the fistula in its posterior aspect. The artery and vein below the level of the fistula appeared essentially normal in size.

**CASE 3** Ferdinand LePage, a 28 year old colored male, was admitted to the Passavant Hospital in April, 1941, for treatment of a type 2 lobar pneumonia. The presence of an arteriovenous fistula in the left femoral region was readily detected during a cursory examination and accounted for certain cardiovascular findings which will be described later.

During his convalescence, a more detailed history revealed that he had been admitted to the Charity Hospital of Louisiana at New Orleans 3 years previous for treatment of a gunshot wound of the left groin. The bullet had entered the groin, passed through the bladder, and had lodged in the right side of the pelvis. Information obtained from the hospital disclosed that following closure of the bladder perforations it was necessary to ligate the femoral artery and vein through a left inguinal incision to

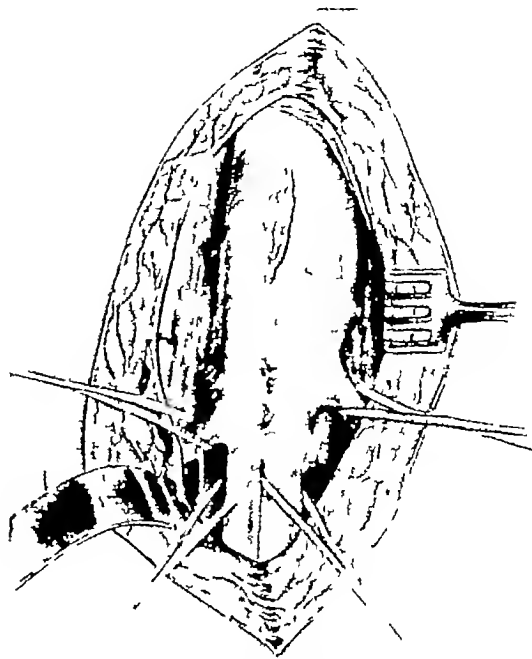


Fig 3 Illustration of the findings at operation in Case 1. The fistula is just proximal to the profunda femoris branch of the femoral artery. The tapes are around the long saphenous and femoral veins on the left side and the profunda femoris and superficial femoral arteries on the right.

control bleeding which had become pronounced during the suprapubic operation. He made an uneventful recovery and was dismissed to the dispensary where it was subsequently found that he had developed a femoral arteriovenous fistula. The heart was enlarged, with systolic murmurs over the entire cardiac area, but there was no evidence of cardiac embarrassment. Operation was deferred to permit the development of a more adequate collateral circulation. He was apparently having no symptoms and did not return.

Physical examination at the Passavant Hospital showed the patient to be a well developed male. The findings referable to the cardiovascular system showed enlargement of the heart with the apex impulse in the 6th left intercostal space, 3 centimeters lateral to the midclavicular line. There was a to and fro murmur over the aortic area and a loud blowing systolic murmur over the mitral area. The pulse rate was one hundred beats per minute with a "water hammer" impulse. The blood pressure was 135 millimeters of mercury systolic and 60 millimeters diastolic. Obliteration of the fistula by digital pressure increased both the systolic and diastolic levels to 145 and 90 millimeters, respectively, and caused the pulse rate to decrease 20 beats per minute.

The abdomen was soft. The liver edge was palpated 2 fingerbreadths below the costal margin.





Fig. 4. Venogram. Case 2. The femoral vein is visualized up to the level of the lesser trochanter of the femur. Above the shadow stops abruptly. Some of the superficial collateral veins are also seen.

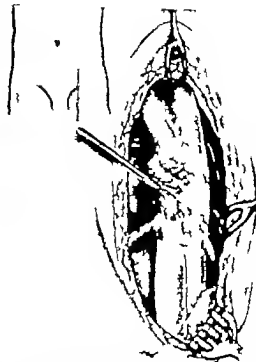


Fig. 5. Illustration of the femoral artery and vein in Case 1. The dense fibrous tissue just above the knee saphenous vein and the profunda femoris artery indicating the level of the fistula.

There are several operative scars: one midline anopubic scar, bilateral inguinal herniorrhaphy scars, and a second scar in the left inguinal region where the femoral vessels had been ligated.

The left leg was entirely normal in external appearance, though swelling or varicosities and no increase in the measurements when compared with the right leg. A marked thrill and bruit was present over the femoral triangle. Pulsations were palpable over the dorsalis pedis artery and could be made to disappear by compression of the fistula.

Venograms (Fig. 6) were made by the injection of 5 cubic centimeters of 30 per cent diodrast solution into the short saphenous vein in an effort to visualize the level of the fistula and the collateral venous return. The media hill both the femoral and long saphenous veins, stopping abruptly at the level of the greater trochanter. From there numerous fine streaks were seen to extend toward the pelvis, appearing even in the region of the right hip.

Operation consisted of quadruple ligation of the common femoral vessels and excision of the segment containing the fistula. The long saphenous and femoral veins were found to be slightly dilated at their juncture and were lost immediately above this in a dense mass of fibrous tissue. The common

femoral artery and its profunda branch were identified at about the same level. They appeared to be about normal size with the exception of stricture of the common femoral artery where it passed lateral to the fibrous mass. The artery was only partially occluded and pulsed normally throughout the entire exposed length. The fistula (Fig. 7) as found above the fibrous mass and just below the level of Poirart ligament no blood could be seen swirling from the common femoral artery into the dilated common femoral vein. There are several small arteries and veins which communicated with the fistulous portion.

On examination of the specimen after removal, the artery above the fistula was found to measure 1 centimeter in diameter and the vein 7 centimeters. The fistula measured 4 centimeters. The common femoral vein (Fig. 8) was completely occluded just below the level of the fistula and apparently did not communicate with the orifice, as well as the stricture of the artery found at the same level, as evidently the result of the ligation at the time of injury.

While the location of an arteriovenous fistula is usually readily apparent on physical ex-



Fig 6 Venogram of the involved leg in Case 3. The media fills both the femoral and long saphenous veins, stopping abruptly at the level of the great trochanter. There are numerous fine streaks extending from this point toward the pelvis, appearing even in the region of the opposite hip.

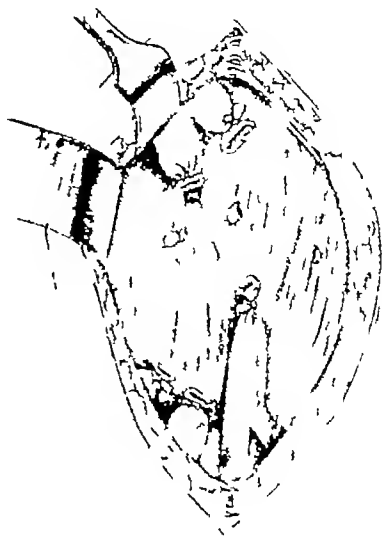


Fig 7 Illustration of the completed operation in Case 3. The proximal stumps of the common femoral artery and vein are seen at the upper angle of the incision, while the stumps of the long saphenous and superficial femoral veins on the left and the distal segment of the common femoral artery on the right are seen at lower angle of the incision.

amination, this is not always the case. The physical signs may be inadequate or even confusing when the fistulas are small, multiple, or when they are situated in the upper mediastinum or pelvis. Venography should be of value in such instances, for in each of the 3 cases cited above, it indicated the level of the fistula as verified at operation.

Arteriography has been used for this same purpose, and several reports have appeared in the literature since Horton first called attention to its value. While we do not suggest that venography be used to supplant arteriography, there are instances in which it may be the only method applicable, such as for the demonstration of fistulas at or proximal to the roots of the extremities, where injection of the artery above the level of the fistula would be difficult or even impossible because of its anatomical position. Venography might even be used in conjunction with arteriography when the presence of multiple fistulas is suspected. In cases in which either method could be used, venography has the advantage

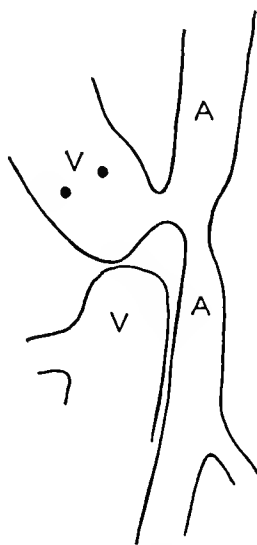


Fig 8 Diagram of the findings in Case 3 to show the complete occlusion of the common femoral vein and the stricture of the common femoral artery just below the level of the fistula.

of permitting the use of media which are inert when injected into the venous circulation and which are readily excreted by the kidneys.

An interesting observation demonstrated by venography in one case was the effect on the extremity of ligation of the common femoral vein at the time of the injury. Brooks has stated that "If from traumatism or in the course of any operation it becomes necessary to ligate a large artery, simultaneous ligation of the concomitant vein should always be considered. If the common femoral artery is ligated I am inclined to believe that it is wiser to close the wound without ligating the vein to watch the extremity carefully for signs of impending gangrene and to ligate the vein only after such signs are evident. In these instances the probable immediate beneficial effects in preventing gangrene must be balanced with the possible remote ill effects of chronic venous stasis." In Case 3 ligation of the common femoral artery and vein at the time of injury 3 years before was not followed by the development of varicosities and edema. The collateral venous circulation was demonstrated by venography and consisted of numerous small venous channels which led directly from the site of ligation into the veins of the pelvis. This is in sharp contrast to the 2 other cases in which the collateral was through numerous dilated and tortuous superficial veins. Although it is impossible even to attempt a generalization from 1 case it is

worthy of note that this case was the only one of the 3 in which there were no varicosities or edema, and would at least suggest that ligation of the vein distal to the fistula at the time of injury might exert the same beneficial effect on the limb that proximal ligation exerts on the heart.

#### SUMMARY

1. Three cases of arteriovenous fistula of the common femoral vessels are reported in which venography was proved to be a reliable means of locating the level of the fistula.

2. Studies of the venograms in each instance showed the vein distal to the fistula to be normal.

3. The venograms demonstrated a marked difference in the collateral venous circulation between 1 case in which the vein had been ligated distal to the fistula at the time of injury for control of hemorrhage and 2 cases in which this had not been necessary.

4. Ligation of the vein distal to the fistula appears to have the same beneficial effect on the extremity that ligation proximal to the fistula has on the heart.

#### REFERENCES

1. HALL, GUY W. *Arteriole scind* 344, 34, 56.
2. BACON, B. L. *Arch Surg* 920, 9, 724.
3. CALLANDER, CLARE L. *Ann Surg* 925, 71, 419-450.
4. DOUGHERTY, JOHN, and HOLT, A. JOHN. *Surg Gyn Obst* 915, 7, 607-70.
5. HOLT, A. *Extrac Arteriovenous aneurysm* P. 17. New York: The Macmillan Co. 1917.
6. HORTON, B. T. *Am J Sl Sc* 934, 87, 649-653.

# RATE OF ABSORPTION AND CALLUS<sup>1</sup> STIMULATING PROPERTIES OF COW HORN, IVORY, BEEF BONE AND AUTOGENOUS BONE

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**D**URING recent years numerous authors have reported unsatisfactory results following the use of metal internal splints in the open reduction of fractures. For this reason considerable interest has been directed toward the determination of a more satisfactory substitute for the autogenous bone graft. The majority of the papers appearing in the literature have described experimental and clinical results obtained by means of various organic animal substances which have been used as internal splints.

Boliarsky, Dahl-Iversen, Fowler (12, 13), and Lever, have supported the use of cow horn. In 1934 Fowler (12, 13), presented evidence to show that cow horn stimulates a fractured bone to produce an excessive amount of callus. He indicated that because the horn is tough and firm but at the same time flexible and not brittle it is very adaptable for use as an intramedullary peg or onlay splint and, because it is absorbed readily, it is satisfactory from a biological aspect. Carrell and Siegling and Fahey are of the opinion that cow horn is not absorbed rapidly and that it is not a satisfactory substitute for the autogenous graft.

Ivory screws, plates, pegs, and inlays have been used to a considerable extent. In 1913 Magnuson described the following advantageous characteristics of ivory in bone: it swells as a result of the imbibition of water and becomes tightened in position, it does not produce necrosis of surrounding bone as metal does, it is absorbed and therefore obviates the need for secondary operations which are necessary sometimes for removal of nonabsorbable materials.

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<sup>1</sup>In this paper the term callus is being used to describe what other authors might refer to as the reaction of bone to a foreign body.

There are numerous references in the literature to the use of beef bone as screws, intramedullary pegs, and extracortical splints. In an experimental study in which intramedullary pegs of boiled beef bone were used in fractured long bones of dogs, Davison and Christopher found that beef bone which remained in contact with the endosteum of the host bone was surrounded by living bone and became solidly embedded in new bone. It was absorbed later and replaced by living bone. Beef bone which was not in contact with endosteum was absorbed rapidly but was not replaced by living bone.

Numerous papers in the literature compare the autogenous and homogenous bone pegs. Brooks and Hudson established experimental bone defects in right and left bones of dog extremities and bridged these defects with homogenous bone in one group of dogs and autogenous bone in the other. They found that the defect was repaired in 84.8 per cent of the cases in which autogenous bone was used and in 76.8 per cent of the cases in which homogenous bone was used.

In an analysis of these papers and a review of other literature dealing with internal splints, it was found that no paper contained definite information based upon a well controlled experiment concerning the comparative rates of absorption and callus stimulating properties of the substances mentioned. In most instances deductions concerning cow horn and ivory were based upon observations of their use in fractured bones. When internal splints are used to fix the fragments of a fractured bone the rate of absorption of the splint, the callus formed about it, and the degree to which it is incorporated in new bone are all affected by (1) the nature of the fracture, (2) the degree of immobilization, (3) the position of the splint with respect to the cortex



Fig. Photograph of dog femur (Experiment 27) 97 days after operation. The ivory peg, *I* and cow horn peg, *H* show no signs of absorption. The extracortical portions of the beef bone peg, *BB* and the autogenous peg, *A* have been absorbed. *E* is an empty hole.

(Intramedullary, intracortical or extracortical position) and (4) the damage to the blood supply about the splint as a result of the fracture. As no well controlled experiment has been described from which conclusions could be drawn concerning the comparative rates of absorption of cow horn, ivory, beef bone and autogenous bone in the medullary cavity in the cortex and outside of the cortex of long bones the following experiments were performed in an effort to solve the problem, to make observations concerning the comparative amounts of callus formed about the respective materials, and to study the degree to which the materials were incorporated in the host bone.

#### PROCEDURE

Slightly tapered cylindrical pegs  $\frac{3}{16}$  inch long and  $\frac{1}{16}$  inch in diameter in the middle were prepared from ivory, cow horn and beef bone. In a few instances (noted in Table I) the ivory pegs were boiled for 2 hours preceding sterilization in the autoclave. Dogs and rabbits were anesthetized by means of sodium barbital or nembutal given intraperitoneally. The skin was prepared for aseptic surgery by

shaving, scrubbing with green soap and application of iodine and alcohol. The proximal end of one fibula was exposed and after the muscles were stripped from it a portion was excised.

When dogs were used two autogenous pegs identical in shape and size with the cow horn, ivory and beef bone pegs were carved from the piece of fibula. On the same side as that from which the piece of fibula was excised, the lateral surface of the femur and the anterior surface of the radius distal to the insertion of the supinator muscle were exposed. Four holes,  $\frac{1}{16}$  inch in diameter were drilled through the bone cortex into the medullary cavity. These holes were arranged longitudinally along the lateral surface of the femur and along the anterior surface of the radius about  $\frac{3}{16}$  inch apart. One each of the autogenous, ivory, cow horn, and beef bone pegs was inserted respectively into the 4 holes in the femur and the radius. All of the pegs were fitted to the holes by cutting off the end with the smallest diameter so that approximately  $\frac{1}{16}$  to  $\frac{1}{8}$  inch of the tapered peg protruded into the medullary cavity. The end which projected outside of the cortex was cut so that it protruded approximately  $\frac{1}{16}$  to  $\frac{3}{16}$  inch. In this way there were intramedullary, intracortical and extracortical portions of each peg. The incisions were all closed with catgut in the fascia and a linen subcuticular stitch in the skin.

When rabbits were used the same procedure was followed except that the piece of fibula was carved into one peg and the radius was not used.

In a few instances, as shown in Table I by a degree sign ( $^{\circ}$ ) a fifth hole was drilled and left empty as an additional control. The order of the pegs with respect to each other, the nutrient artery and proximal end of the bones, was changed in various experiments to avoid misinterpretation of results because of the difference in blood supply to the various parts of a bone. Eight rabbit experiments and 21 dog experiments were performed in all.

These experimental animals were observed from 7 to 411 days before autopsy. X-ray films were made at frequent intervals during the postoperative period to study the forma-

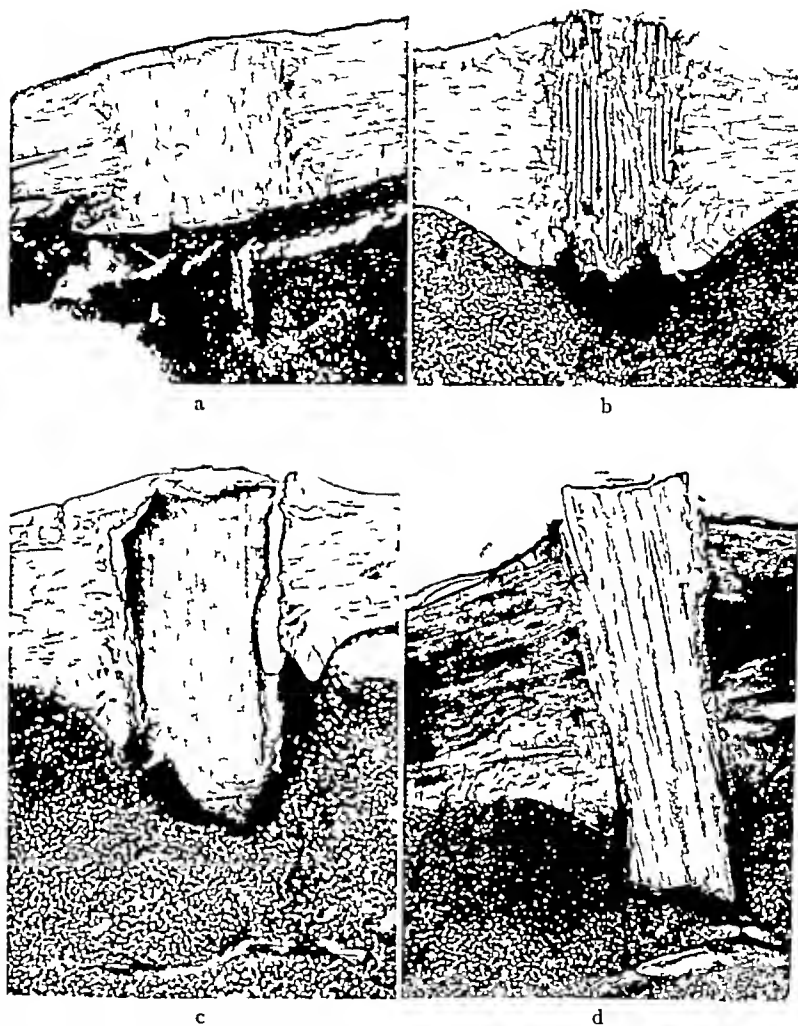


Fig 2 Microscopic sections of the pegs and host bone 181 days after operation (Experiment 9) The autogenous peg, a, and the beef bone peg, b, are completely absorbed except for the intracortical portions There is considerable incorporation of the pegs into the host bone Small processes of host bone can be seen extending into the pegs The extracortical portion of the ivory peg c, is absorbed The cow horn peg, d, shows no absorption There is a definite line of demarcation between the host bone and the ivory and beef bone pegs

tion of callus around the pegs Photographs were made of the experimental bones after death and 15 of the specimens were decalcified, imbedded in celloidin, and sectioned

The gross specimens, microscopic preparations, and x-ray plates were all examined by two impartial individuals besides the author to determine the extent of absorption of the

various pegs Each examiner recorded independently the degree of absorption on a scale where "7+" indicated complete absorption and restoration of contour of the host bone (see Table I)

#### RESULTS

An analysis of these data shows that absorption of the extracortical portion of both

TABLE I—RECORD OF EXPERIMENTS

Experiment number	Duration of experiment—days	Animal	Type of material	Number of pegs	Position of pegs				Absorption of pegs				Callus formation			
									A	B	I	H	A		I	H
6		Rabbit	Barbital		H	B	A	I								
		Rabbit	Barbital		H	I	B	A	+	+						
153	96	Dog	Nonbarbital		H	B	A	H	+	+						
96	96	Dog B	Nonbarbital		A	I	B	H					+	+		+
105	70	Rabbit	Nonbarbital		B	B	I	A	H				Four Insertion of Pegs			
5	100	Dog	Nonbarbital		H	H	A	B	+	+	+				+	
	100	Dog B	Nonbarbital		A	H	H	B	+	+	+		+			+
195	17	Dog	Nonbarbital		A	H	I	B	+	+			+	+		
103	127	Dog B	Nonbarbital		A	H	I	B		+			+	+	+	+
36	150	Rabbit	Nonbarbital		H	A	B	H	+		+		+	+	+	+
58	17	Dog	Barbital		A	B	I	H	+	+			+		+	+
63	181	Rabbit	Barbital		A	H	I	B	+	+			+		+	+
17	197	Dog	Nonbarbital		A	H	B	H		+			+	+		
18	197	Dog B	Nonbarbital		A	H	B	H	+	+	+		+	+	+	+
	190	Dog B	Nonbarbital		H	A	H	I	+	+			+	+	+	
55	190	Dog B	Nonbarbital		I	B	A	H	+	+	+		+	+	+	
19	270	Rabbit	Barbital		H	I	B	A	+	+	+	+				
196	18	Rabbit	Nonbarbital		A	I	H	B	+	+	+		+	+	+	
	100	Dog	Nonbarbital		H	B	A	H	I	+	+	+	+	+	+	+
25	100	Dog B	Nonbarbital		H	B	H	I	A	+	+	+	+	+	+	+
	11	Dog	Nonbarbital		H	A	O	I	+	+	+	+				
18	114	Dog B	Nonbarbital		H		B	I	+	+	+	+	+	+		
	100	Dog	Nonbarbital		H	A	B	I	+	+	+	+	+	+		
14	70	Dog B	Nonbarbital		H		B	I	+	+	+	+	+	+	+	+
29	153	Rabbit	Barbital		I	H	B	B	+	+	+	+	+	+	+	+
	160	Dog	Barbital		B	B	A	H	I	+	+	+	+	+	+	
	177	Dog	Barbital		I	B	H	A	+	+	+	+	+	+	+	
	41	Dog	Barbital		A	H	I	B	+	+	+	+	+	+	+	+
	Lost	Dog	Barbital		H	I	A	B					+	+	+	
Totals rabbits, dog femora, 9 dog ends									90+	10+	11+	+	11+	10+	17+	12+

5, Specimens which were prepared histologically. B, Rabbit. Empty drilled hole. Inserted.  
Positions: H, most proximal, A, most distal. A, Anteroposterior. B, B, best bone. I, ivory. H, bone.

the autogenous and beef bone pegs had begun at 35 days. The ivory pegs which had been boiled were partly absorbed as early as 100 days after operation, but the pegs which were not boiled showed no signs of absorption until 174 days after operation. The first sign of absorption of any of the cow horn pegs was noted 270 days after operation. During 367 postoperative days the rate of absorption of autogenous, beef bone ivory and cow horn pegs follows the ratio autogenous, 9 beef bone 7 ivory 3 and cow horn 1. Figure 1

Is a picture of a dog femur 197 days after operation (Experiment 27). In this picture the marked absorption of the autogenous and beef bone pegs in contrast to the very slight absorption of the cow horn and ivory pegs can be noted.

In Figure 2 the degree to which the various materials became incorporated in the host bone 181 days after operation can be observed. In the bone in which cow horn was used, a very distinct demarcation exists between the host bone and peg. The same is



Fig 3 The microscopic findings at the point of juncture between host bone and pegs 367 days after operation (Experiment 3) The peg is on the right in each instance The arrow indicates the line of demarcation The autogenous peg, a, is united with the host bone The horizontal haversian canals of the host bone have formed connections with the vertical canals of the peg Revascularization of the peg is occurring through these connections The beef bone peg, b, is united with the host bone and similar revascularization has occurred The ivory peg, c, and the cow horn peg, d, are not united with the host bone There are no canals in cow horn or ivory and consequently absorption and replacement of these substances can take place only on the surface of the peg

true in the case of the ivory, c The opposite is true when beef bone, b, and autogenous bone, a, were used In these cases it is difficult to locate the line of demarcation between host

bone and peg The horizontal haversian canals characterize the host bone while the vertical canals are more distinct in the autogenous and beef bone pegs





Fig. 4. An x-ray plate of dog femur 33 days after operation (Experiment 1). Considerable callus can be seen around the cow horn peg, *H*; the ivory peg, *I*; and the beef bone peg, *B*. There is very little callus around the autogenous peg, *A*.

Figure 3 reveals the microscopic findings 367 days after operation (Experiment 3). In Figure 3a the definite union between the autogenous graft and host bone is apparent. The horizontal haversian canals of the host bone have formed connections with the vertical canals of the graft. Revascularization of the graft occurs through these connections. Figure 3b reveals an enlargement of the haversian system of the beef bone peg. Many of the canals have changed direction as they have enlarged. Communications form between the vertical canals of the peg and the horizontal canals of the host bone. The canals in the peg enlarge as the beef bone is absorbed around the vessels in the canals and the canals change direction as new bone is formed to replace the beef bone. Figure 3c and d reveal a different situation. There are no canals in ivory or cow horn and consequently absorption and replacement of these substances can take place only on the surface of the peg where the cortical portion of host bone joins the peg. Thus we find that beef bone is incorporated into the host bone almost as readily as autogenous bone. Cow horn and ivory remain unincorporated.

The determination of the comparative amounts of callus formed about the pegs was made from a study of the x-ray plates. This study was also made by the 2 observers mentioned earlier in the paper. The amount of callus was recorded as 0 to 4+ by the three of us independently and our results were averaged and recorded in Table I. The total number of positives recorded for each peg is: autogenous, 34; beef bone, 46; ivory, 53; and horn, 52. These figures show that there is 1.5 times as much callus formed around the pegs of ivory and horn as there is around the autogenous peg. There is 1.35 times as much callus around the peg of beef bone. The typical arrangement of callus around the pegs can be seen in Figure 4.

#### SUMMARY AND CONCLUSIONS

1. In long bones foreign substances which are located within bone cortex are absorbed slowly. Substances within the medullary cavity are absorbed more rapidly and materials which are extracortical in position are absorbed most rapidly.

2. Absorption of the extracortical portion of autogenous and beef bone pegs is perceptible after 1 month. The same is perceptible in ivory (not boiled) pegs after 6 months and cow horn pegs after 9 months.

3. When the amount of callus formed around an autogenous peg is considered as a unit, there is one third more callus around a beef bone peg and one half more callus around ivory or cow horn pegs.

4. There is no firm union formed between ivory or cow horn pegs and the host bone. Microscopically it appears that there is definite bony union between the autogenous or beef bone pegs and the host bone.

5. Beef bone is a much better substitute for autogenous bone grafts than ivory or cow horn.

#### REFERENCES

1. BAILEY, H. Birmingham M. Rev. 97, 13.
2. BOON, WOLFE, L. Med. Vet. St. Petersburg 27, 83.
3. BOLIVAR, N. N. Vet. Med. 97, 9, 144.
4. BARNETT, A. G. Surg. Gyn. Obst. 92, 30, 200.
5. BRONKH, B. and H. DEER, W. N. Arch. Surg. 220, 284.
6. CARROLL, W. B. Surg. Gyn. Obst. 25, 43, 67.

- 7 CUNNINGHAM, W Wisconsin M J, 1924, 23 224
- 8 DAHL IVERSEN, E Arch klin Chir, 1930, 158 680
- 9 Ibid, 1931, 165 345
- 10 DANIS, R. Bull Acad roy med Belgique, 1936, 1 88
- 11 DAVISON, C, and CHRISTOPHER, F Surg Gyn Obst, 1924, 38 534
- 12 FOWLER, E B Illinois M J, 1934, 65 56
- 13 Ibid, 1934, 66 231
- 14 GAGLIO, V Ann ital chir, 1932, 11 603
- 15 GAUDIOSO, E T Polclinico, 1924, 31 735 Abstr J Am M Ass, 1924, 83 227
- 16 GAZZOTTI, L G Chir org movim, 1923, 7 311
- 17 HARRIS, I B Ohio M J, 1925, 21 818
- 18 HENDON, G A South M J, 1925, 18 801
- 19 HENDERSON, M S J Am M Ass, 1920, 74 715
- 20 LEXER, E W Deut Zschr Chir, 1932, 236 234
- 21 MAGNUSON, P B J Am M Ass, 1913, 61 1514
- 22 MENEGAUX, G, MOYSE, P, and ODIETTE, D Presse med, 1934, 42 658
- 23 ODI, F Lyon chir, 1926, 23 296
- 24 RUHL, J Arch orthop Unfallchir, 1934, 34 615
- 25 SIEGLING, J A, and FAHEY, J J J Bone Surg, 1936, 18(n s) 439
- 26 TARNOWSKY, G de Surg Gyn Obst, 1916, 22 610,
- 27 Ibid, 1922, 35 342
- 28 TROELL, A Hygiea, 1923, 85 79
- 29 WERWATH, K Chirurg, 1930, 2 1126

# CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEOESOPHAGEAL FISTULA

## Extrapleural Ligation of Fistula and End-to-End Anastomosis of Esophageal Segments

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THE most frequent type of congenital anomaly of the esophagus consists of a blind upper esophageal segment and a lower segment communicating with the trachea. The surgical treatment of this anomaly has until recently been unsuccessful. The reasons for failure are primarily due to the deep location and extent of the anomaly, the technical difficulties encountered in correcting it, and the complications occurring before and after operation.

In the surgical management of congenital atresia of the esophagus associated with tracheoesophageal fistula, two general plans of treatment have been used. One plan the indirect attack, aims to circumvent the anomaly by the use of staged operations. In principle the indirect plan consists of (1) a gastrostomy for permanent feedings, (2) ligation or exteriorization of the distal esophageal segment to prevent the regurgitation of gastric contents into the trachea and bronchi, and (3) exteriorization of the upper esophageal segment to allow for drainage of pharyngeal secretions onto the skin. The various methods of application of this plan will be described later in this report. The other plan of attack is the direct one whereby the continuity of the esophagus is restored. The operation consists of a one stage extrapleural exposure of the anomaly with ligation of the tracheoesophageal fistula and simultaneous anastomosis of the two esophageal segments. The advantage of the direct plan is that if successful the patient is able to swallow normally.

During the last 7 years 15 infants with congenital atresia of the esophagus have been admitted to the University of Michigan Hospital. A tracheoesophageal fistula was present in 14 of the 15 cases, the anomaly being of the type 3 B as described by Vogt. In the remaining case air was not present in the stomach, but the absence of a fistula could not be definitely ascertained as the patient died without operation or autopsy. This report will be concerned with the experiences encountered in these patients, with particular reference to the findings in 9 patients in whom a thoracic exploration has been done. One case with a successful reconstruction of the esophagus will be reported in detail.

### CASE REPORT

J. M. N., 47733, girl, 1 day of age, admitted to the University Hospital on March 4, 1941. The patient was referred by Dr. Moses Cooperstock of the Northern Michigan Children's Clinic, Marquette, Michigan, with the diagnosis of congenital atresia of the esophagus with tracheoesophageal fistula.

The infant had presented evidences of hemorrhagic disease of the newborn on the day following delivery. Bleeding had occurred from the mouth and rectum, and the obstetrician, Dr. J. H. Fyfe of Marquette, Michigan, had administered vitamin K. Fluid taken by mouth immediately regurgitated with associated emesis. A catheter introduced under roentgenoscopic control could not be passed beyond the junction of the upper and middle third of the esophagus. Roentgenogram after the administration of lipiodol by mouth (Fig. 1) revealed obstruction of the esophagus at the lower portion of the upper third. A large amount of air, as noted in the stomach and intestines. A roentgenogram made about 1 hour later showed lipiodol thus in the tracheobronchial tree. A small amount of lipiodol had passed from the trachea through the tracheoesophageal fistula and into the stomach (Figs. 2 and 3).

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Presented at the Central Surgical Association, Chicago, Illinois, February 17-18, 1941.



Fig 1 a and b, Frontal and lateral roentgenograms following the ingestion of lipiodol show the blind dilated upper esophageal segment. The stomach and intestines are distended with air indicating the presence of a tracheoesophageal fistula. c, One hour later. Retained lipiodol is seen in the upper esophageal segment. Some of the lipiodol has overflowed into the trachea and bronchi, and a small

amount has entered the stomach by way of the tracheoesophageal fistula (aspiration of the opaque medium by means of a catheter immediately after the film studies were made would probably have prevented the overflow into the trachea). Preadmission roentgenograms were furnished by courtesy of Dr M Cooperstock, Marquette, Michigan.

Treatment at the Northern Michigan Children's Clinic consisted of administration of fluids subcutaneously and intravenously. In transporting the patient from Marquette to Ann Arbor, a distance of approximately 500 miles, Dr Cooperstock arranged with two local physicians en route for the administration of parenteral fluids so that the child would not become too dehydrated during the long automobile trip.

Examination revealed a well developed infant weighing 8 pounds and 4 ounces. The rectal temperature of 103 degrees F appeared to be the result of moderate dehydration which was evident by the dryness of the mucous membranes of the mouth and tongue. A considerable amount of thick mucus was present in the pharynx. Many loud rhonchi over both lung fields disappeared after aspiration of mucus from the pharynx. No râles were heard and there was no evidence of pneumonia or atelectasis. The heart sounds were of good quality. The abdomen was soft and gastric tympany was present on percussion. As the preadmission roentgenograms were not available, a roentgenologic examination of the anomaly was repeated. A catheter introduced under roentgenoscopic control showed a blind upper esophageal segment extending down to the level of the second dorsal vertebra. A small amount of lipiodol was injected, "spot" films were made, and the lipiodol was then aspirated. The lower level of the upper segment was again noted to be at the

second dorsal vertebra. Roentgenograms of the chest and abdomen showed both lung fields to be clear and a large amount of air was seen in the stomach and intestines. In view of the elevated temperature and moderate dehydration, fluids were given to correct the dehydration and operation was deferred. On the following morning, the temperature was normal and the lung fields remained clear, although foamy mucus in the mouth and nose required frequent aspiration. In view of the satisfactory general condition of the infant it was decided to proceed with operation.

*Operation, March 15, 1941. Extrapleural ligation of tracheoesophageal fistula and end-to-end anastomosis of esophageal segments.* With the infant lying on the right side a left paravertebral incision was made, under local anesthesia ( $\frac{1}{4}$  per cent metycaine hydrochloride solution). Local anesthesia was continued until the anastomosis was begun when general anesthesia was necessary. The posterior portions of the 2d, 3d, 4th, and 5th ribs were resected subperiosteally for a distance of approximately 4 centimeters each. The 2d, 3d, and 4th intercostal nerves were resected, the accompanying intercostal vessels were doubly

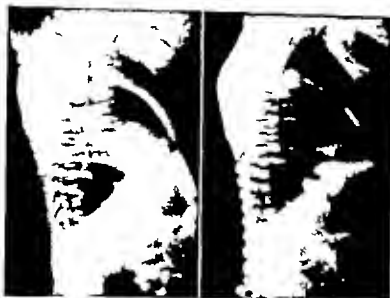


Fig. Stability of the upper esophageal segment is demonstrated in these lateral roentgenograms and 4 hours after the ingestion of lapidol. Roentgenoscopic observations confirmed the wide degree of vertical excursion.

ligated and divided and the intercostal muscles and periosteum were divided (Fig. 3). The costal and mediastinal pleurae were separated from the thoracic wall by blunt dissection, thereby exposing the left subclavian artery extrapleurally. The subclavian artery was displaced forward by an illuminated retractor (Fig. 4). The upper esophageal segment was situated higher than usual so much so that it could not be seen until it had been pushed downward by a catheter introduced through the mouth. A tension suture was placed in the wall of the upper segment. In order to gain adequate exposure of the lower esophageal segment the two uppermost intercostal vessels arising from the aorta were doubly ligated and divided allowing the presenting portion of the aortic arch to be displaced downward forward and medially. The lower esophageal segment measuring about 6 millimeters in diameter was freed up to its point of communication with the trachea (about 0.5–1 cm. above the bifurcation). It was ligated with silk close to the trachea and was divided distal to the ligature. Traction on the tension suture allowed the blind upper pouch to be drawn down to the level of the

distal segment but when the patient strained or cried, the upper segment retracted upward into the neck and out of sight. The tip of the upper segment was opened for a distance corresponding to the diameter of the distal segment and the interior of the two segments was cleaned with a 3000 solution of acriflavine. When an attempt was made to unite the two segments the first suture pulled out due to the forceful upward retraction of the upper segment when the child strained. The tension suture in the upper segment proved to be a fortunate provision, inasmuch as the upper segment again disappeared from view. As it had been opened, it is problematical whether it could have been pushed downward again by a catheter and an attempt to grasp it would have been a blind maneuver. Open drop ether anesthesia was then begun the complete relaxation that was obtained allowed the two segments to be approximated without tension. A single layer of interrupted sutures of plastic silk was used to construct the anastomosis. As the mucosa of the upper segment tended to be everted in one place it was incised with an additional suture. A small rubber drain was placed near to the site of the anastomosis and

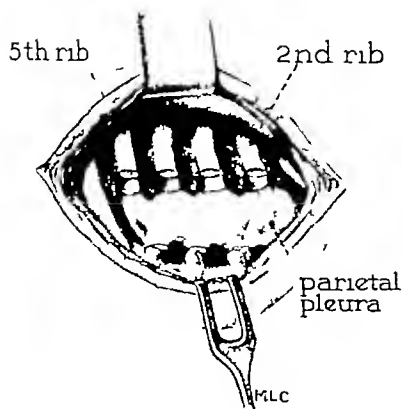


Fig 3

Fig 3 Drawing illustrates the extent of the costal resections. The posterior and posterolateral portions of the 2d, 3d, 4th, and 5th ribs have been resected and the intercostal muscles, vessels, and nerves, and periosteal beds have been divided to expose the parietal pleura.

Fig 4. Diagrammatic drawing to illustrate the left extra pleural exposure of the anomaly. The parietal pleura has been separated from the thoracic wall. The subclavian

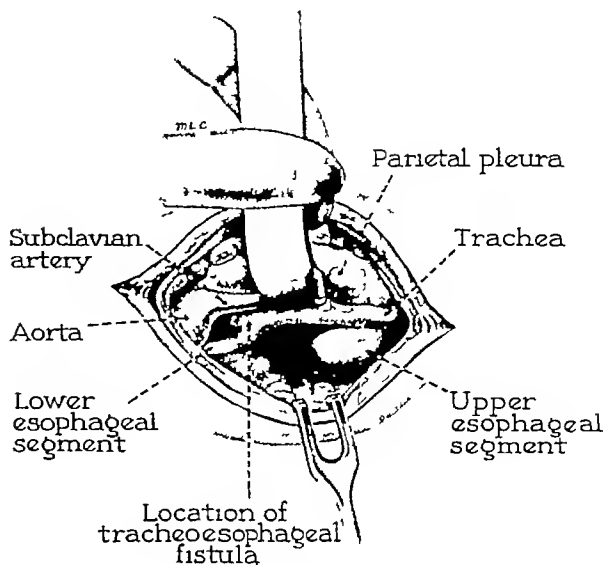


Fig 4.

artery is being retracted forward, exposing the upper esophageal segment. The uppermost intercostal artery has been ligated and divided to allow the descending portion of the aortic arch to be displaced forward. The origin of the lower esophageal segment is seen. The drawing shows an exposure of the entire operative field, whereas at operation it is possible to obtain an exposure of only a portion of the operative field at any one time.

was brought out through the lower angle of the incision. The wound was closed in layers with interrupted silk sutures. The skin edges were closely approximated around the drain. As an added precaution to prevent the sucking of air into the extrapleural space, a vaseline gauze dressing was applied. Although the parietal pleura was extremely thin, it was not opened at any time during the operation. The infant's condition was good at the end of the operation.

**Postoperative course.** Upon return to the nursery, the child was cyanotic and the respirations were rapid and slightly labored. An oxygen tent was used for the following 14 days because of the return of cyanosis whenever the infant was removed from the tent. As a prophylactic measure against infection, 0.25 grams of sulfathiazole was given every 6 hours by rectum. On the day of the operation, 300 cubic centimeters of normal saline solution was given subcutaneously. Five hundred cubic centimeters of saline solution was given on the 1st postoperative day and 200 cubic centimeters on the 2d day. Edema of the legs and genitalia occurred on the 2d postoperative day. As generalized edema had developed

on the 3d day, fluids were withheld. During the first several days following operation, a considerable amount of mucus in the pharynx required aspiration at intervals. Coarse rhonchi were evident at times on auscultation of the chest and an occasional cough was noted. There were no physical signs of bronchopneumonia, and roentgenograms on the first and third days likewise showed no evidence of pneumonia.

On the 4th postoperative day, several drops of sterile water were placed in the infant's mouth every hour while awake. She appeared to be hungry and sucked her fingers much of the time, but she did not choke on the saliva. On the 6th postoperative day, carbon dioxide oxygen inhalations were started because of persistent cyanosis. Foamy secretions suggestive of saliva were seen around the rubber drain in the operative incision on the seventh postoperative day. The wound showed evidence of infection. A small amount of dilute methylene blue was given by mouth, but the dye could not be seen in the wound or on the dressing. The child was then given a small amount of lipiodol under roentgenoscopic control. The oil passed down to the site of the anastomosis where the column of oil bifurcated and practically all the oil extravasated into the operative wound. Only a small amount of the lipiodol continued down into the distal esophagus.

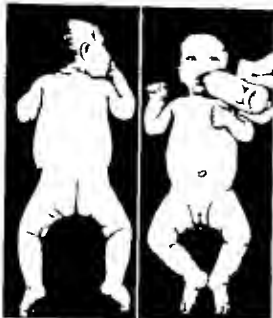


Fig. 5. Photographs of patient 3 months after closure of tracheoesophageal fistula and end-to-end anastomosis of the esophageal segments. The thoracic wound has been healed for 3 months, and the gastrostomy wound has been healed for 3 1/2 months.

The feedings were discontinued by mouth and on the 6th postoperative day a gastrostomy was done by Dr. H. K. Ransom. In the week preceding the gastrostomy the infant received 75 cubic centimeters of plasma on the 4th postoperative day, 75 cubic centimeters of plasma on the 5th postoperative day and 85 cubic centimeters of citrated blood on the 6th postoperative day. Fluids had been continued mostly by subcutaneous saline infusions, supplemented by two intravenous infusions of 1 per cent glucose. On the day following the gastrostomy the hemoglobin was 56 per cent, the red blood cells, 3,000,000 and the plasma proteins, 3.8 per cent, the albumin fraction being 5 per cent and the globulin fraction 3 per cent. I view of the anemia and low serum proteins, second transfusion of 80 cubic centimeters of citrated blood was given. A moderate degree of edema persisted for the next few days, but disappeared after 60 cubic centimeters of plasma had been given on the 3th postoperative day.

Feedings by the gastrostomy tube were started on the day following the gastrostomy and consisted of small amounts of 5 per cent glucose every 4 hours, followed shortly by formula of evaporated milk, Karo syrup and water. The feedings were increased to ounces every 3 hours. Curdled milk particles escaped from the thoracic wound 3 days after the gastrostomy feedings were begun. At this time catheter was introduced by mouth and advanced

into the esophagus, in order to determine whether the channel at the site of the anastomosis could be probed in the hope that a thread could be introduced into the stomach. However the catheter emerged from the wound in the chest. The gastrostomy feedings were reduced to three-quarters of an ounce every 4 hours, and regurgitation of the feedings into the thoracic wound was thereby prevented. On the 20th day following operation, and on the 24th day following the gastrostomy the child regurgitated through the mouth approximately one-quarter of an ounce of the formula that had been given by the gastrostomy tube. This finding demonstrated the patency of the lumen of the esophagus. On the following day lipiodol was again administered by mouth and the opaque medium was seen to pass down to the site of the anastomosis. The lipiodol then deviated to the left and passed downward into the stomach. A lipiodol was seen in the extra pleural wound. From this observation it appeared that the esophageal fistula had become closed by secondary intention healing. The thoracic wound was packed daily with narrow strip of gauze and was completely healed 3 months after operation.

Feedings by mouth were started on the 1st postoperative day. The child eagerly took 1 cubic centimeters of water every 4 hours by mouth. On the following day the feedings were increased to 5 cubic centimeters of water every 4 hours. Three days later when the child erupted, gas could be heard purring from the infant's mouth. A formula was then started by mouth, and the amount of the feedings was gradually increased. During this period of increased feedings by mouth, the feedings through the gastrostomy tube were simultaneously reduced. Roentgenographic and roentgenoscopic examinations of the esophagus were made on the 1st day of rogar on the 38th postoperative day. The rogar passed down to a point approximately the junction of the upper and middle thirds of the esophagus where there was temporary hesitation of the opaque mixture. The upper part of the esophagus was moderately dilated. The patient was then fed a small amount of formula and as the milk mixed with the rogar the mixture ran down into the distal esophagus. A marked narrowing was present at the site of the anastomosis where the lumen of the esophagus deviated to the left and posteriorly. There was, however, no evidence of leakage. Roentgenograms were made immediately following the fluoroscopic observation and all the opaque mixture had passed into the stomach at the time the films were made. The gastrostomy feedings were discontinued on the 39th day as the infant was able to take all the necessary feedings by mouth. The gastrostomy tube was removed on the 42d postoperative day and the gastrostomy wound was completely healed 1 week later (Fig. 5).

The infant's weight decreased from 8 pounds and 4 ounces on admission to a minimum of 7 pounds and 4 ounces during the 4th week of hospitalization. During the 5th week, the weight began to increase.

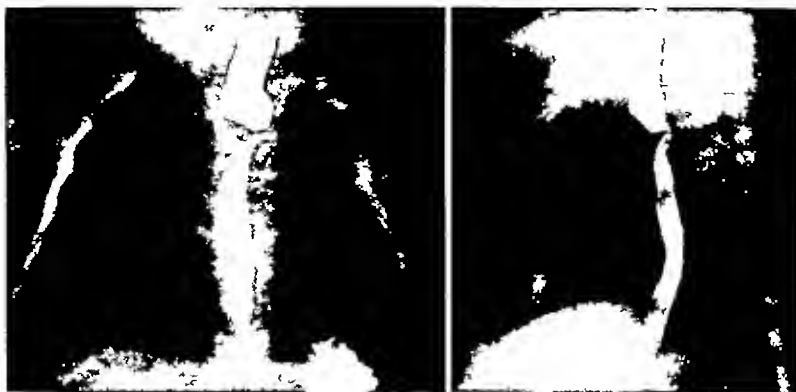


Fig 6 Roentgenographic examination following the ingestion of rugar 4 months after operation. The upper portion of the esophagus is moderately dilated, and a short narrow stricture is present at the site of the anastomosis as a result of healing by second intention. The lumen of the esophagus in the region of the stricture has a pronounced cork-screw curve, as seen in the frontal projection.

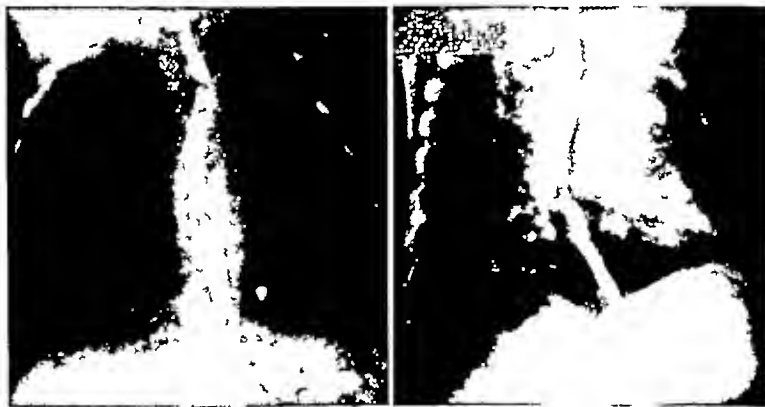


Fig 7 Roentgenographic examination 11 1/4 months after operation. There is no dilatation of the upper portion of the esophagus. The lumen of the esophagus at the level of the stricture is larger than in Figure 6 and is considerably less curved.

and at 6 months, the infant weighed 12 pounds and 2 ounces. At 11 1/4 months, the time of this report, the weight is 17 pounds. During the 3d and 4th months after operation, the feedings consisted of a formula of evaporated milk, 50 per cent Karo syrup and water. During the 5th month, cereal (Pablum) was started by mouth and has been continued to date. The patient is now receiving a cooked cereal twice daily in addition to strained vegetables and fruits.

The feedings have often been accompanied by an accumulation of mucus in the pharynx and upper esophagus, the mucus interfering greatly with the ability to swallow. These episodes occur several times weekly at irregular intervals and persist during an entire feeding. Usually at the succeeding feeding, the mucus is not noticed, but the tendency for mucus accumulations is strikingly increased during an

upper respiratory infection. To counteract this tendency, the infant has been given small sips of water prior to each feeding with beneficial effects. For a period of several months atropine sulfate (1 drop of a 1:2000 solution) was given twice daily to dry up the pharyngeal secretions. The atropine sulfate proved helpful at first, but later it became less effectual and was discontinued. The episodes of mucus accumulation are becoming less frequent, although, when present, they occur at each feeding during an entire day. Repeated roentgenoscopic and roentgenographic observations have shown a persistence of the stricture at the site of the anastomosis (Fig 6), but the more recent observations show less delay in the passage of the opaque meal at the site of the stricture. Likewise there has been a gradual decrease in the degree of dilatation of the esophagus above the stricture and at the present





FIG. 8 Photograph of patient 3 months after operation.

time there is no kinking of the upper esophagus (Fig. 7). The stricture however is sufficiently tight so that it is believed that subsequent dilatation will be advisable.

#### PREOPERATIVE CONSIDERATIONS

**Diagnosis** The presence of esophageal obstruction is readily suspected from the typical history of inability to swallow fluids and of attacks of choking, dyspnea, and cyanosis during the attempted ingestion of fluids. Examination reveals intermittent accumulations of considerable mucus in the pharynx. The respirations may be partially obstructed when excessive amounts of secretions are present in the pharynx, or if secretions have gained entrance into the tracheobronchial tree. A positive diagnosis of esophageal obstruction is made by roentgenologic examination with an opaque medium or by the inability

to pass a catheter into the stomach. In the presence of a complete esophageal obstruction, the existence of a tracheoesophageal fistula is indicated by the presence of tympany or distention of the upper abdomen on physical examination and by the visualization of air in the stomach on roentgenologic examination. The diagnosis of atresia of the esophagus with tracheoesophageal fistula can also be made by endoscopic examination of the esophagus and trachea, as performed by Tucker and Pendergrass, and Shaw (14). Shaw also employed endoscopy for the removal of retained barium in the tracheobronchial tree and in the upper esophageal segment. Shaw advises that preoperative bronchoscopic examination be done in all cases to determine the type of anomaly but to date we believe that bronchoscopy is not necessary to establish the diagnosis except possibly in those cases without air in the stomach. Also we have not employed bronchoscopic examination as we have felt that it carries certain risks in newborn infants.

**Roentgenographic observations concerning operability** A liquid radio-opaque material is used to determine the level of obstruction of the upper esophageal segment. Iodized oil should be employed instead of a barium suspension, as the barium may cause serious pulmonary complications if it gains entrance into the bronchi. The iodized oil is administered under roentgenoscopic control as it is advisable to limit the amount of oil so that it will not overflow into the trachea. At the conclusion of the roentgen examination the retained oil in the upper esophageal segment is aspirated through a catheter that is introduced for this purpose. The blind end of the dilated upper esophageal segment is usually found at a level between the 1st and 3d dorsal vertebrae. As seen fluoroscopically the upper esophageal segment is not a fixed structure but undergoes a vertical excursion during respiration. During inspiration the upper segment descends to a lower level than on expiration. The amplitude of the excursion is augmented by crying and deep breathing and may be as much as the height of 2 dorsal vertebrae. Roentgenoscopic examination furnishes a more accurate means of determining the length of the upper segment than does

<sup>1</sup>May 1943 The intermittent episodes of accumulation of mucus and regurgitation of food at intervals of 10 to 12 days have continued to occur. Because of these symptoms, an esophagoscopic examination was done by Dr. J. H. Maxwell on August 18, 1943. (Note by other operators 1943) The examination revealed an esophageal stricture at the site of the tracheostomy. The stricture was gently dilated with bougies. On roentgenoscopic examination, mucus later regurgitated through the constricted area without difficulty. Accordingly the esophagoscopic dilatation has not been repeated. The weight was 35 pounds at the time. The patient was discharged from the hospital on December 24, 1943. The patient was examined at the Northern Michigan Children's Clinic on April 1944. The child, as is usual general condition and had been as before several accidents. Although the regurgitation of food at intervals had continued, the weight had increased to 50 pounds. Liquid was administered by mouth, and on roentgenoscopic examination the oil passed through the esophagus without delay. The esophagus dilated to the level of the site of the stricture, but the stricture itself had been present in the earlier films was not seen.

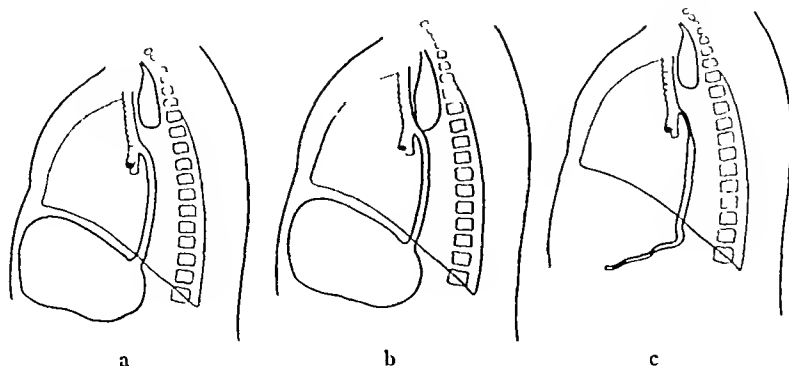


Fig. 9 The drawings illustrate the type of anomalies that have been encountered in 8 of the 15 cases in which the diameter of the lower segment could be determined at operation. a, Air is present in the stomach indicating the presence of a tracheoesophageal fistula. The two esophageal segments are separated from one another, but the diameter of the lower segment is ample for an anastomosis. Three cases. b, Same as drawing a, except that partial muscular continuity exists between the two segments. Two cases. c, The lower segment is contracted for a variable distance below its attachment to the trachea. Three cases. In 2 of these cases air was not present in the stomach (as illustrated). In 1 of the 2 cases the lower segment was too narrow to permit an anastomosis to be made, in the other case an anastomosis was possible after dilatation of the contracted lower segment during operation (see Fig. 10). In the third case, the stomach was distended with air (not illustrated), but the diameter of the lower segment was too narrow for an anastomosis.

roentgenographic examination. If one considers the possibility of operative correction from a study of the films alone, the fact that the upper segment occupies a high position, as seen in the films, is not necessarily a contraindication to surgical reconstruction. Thus in one of our cases, the roentgenograms revealed the upper segment to be situated higher than usual. It apparently extended only as low as the 1st dorsal vertebra. At operation, however, the upper segment was found to extend even lower than usual. In this case, the tip of the upper segment overlapped the lower segment at a level slightly above the bifurcation of the trachea, and the two segments were attached to one another by a partial continuity of their muscle coats. This partial continuity of the musculature of the two segments has been noted in another of the 9 cases that have been surgically explored. In the latter instance the upper segment had a low position (4th dorsal), as seen in the preoperative roentgenograms.

The presence of air in the stomach is indicative of a communication between the trachea and the lower esophageal segment. Although the failure to visualize air in the stomach suggests the absence of a tracheo-

esophageal fistula, this fact is not necessarily true. In 2 of the 3 cases in which air was not seen in the stomach by roentgenologic examination (Cases 12, 14, and 15), an unusually small communication was found to exist between the trachea and a narrow lower esophagus at operation. After dilatation of the greatly contracted lower segment during operation in 1 of the 2 cases (Case 12), it was possible to perform a technically satisfactory anastomosis (Fig. 10) between the two segments. In the other case (Case 15) the lower segment was too small to allow dilatation, and no attempt was made to perform an anastomosis. In the 3d case (Case 14) the exact findings are not known as the infant died without operation and an autopsy was refused.

*Time of operation.* The operative correction of a tracheoesophageal fistula is not a procedure of the utmost emergency. The time at which the operation is undertaken is of secondary importance to the general condition of the patient. The operation should not be delayed unnecessarily, inasmuch as the earlier it is done, the shorter is the opportunity for the development of pneumonia from the aspiration of pharyngeal secretions. It is advisable, however, that the operation should

Leven (7) in 1941 in his most recent article advised interruption of the distal esophagus by a direct extrapleural attack upon the fistulous communication with the trachea instead of interruption of the lower esophagus at its junction with the stomach, inasmuch as the obstruction of the esophagus at its lower level does not allow for drainage from the lower segment except into the trachea. In his most recent patient, he performed a 3 stage procedure. At the first stage (November 1939) a preliminary gastrostomy was made. After recovery from this operation the communication with the trachea was ligated extrapleurally. At the third stage the upper esophagus was mobilized and brought to the skin surface to form a cervical esophagostomy. The patient who was alive and well 18 months following the first operation is the only successful case to date by the indirect approach. Leven expects, at some future time to construct an antethoracic esophagus to establish the continuity of the gastrointestinal tract.

The main disadvantage of the indirect procedures is that they do not attack the problem directly and that the infant is still unable to swallow unless an antethoracic esophagus is constructed by a skin-lined tube or unless the cervical esophagostomy and the gastrostomy are connected with a rubber tube. The indirect type of operation, however is recommended by Leven and Carter as offering a safer approach to the problem than does a single stage extrapleural reconstruction of the esophagus. Carter also believes that his method provides an ideal type of gastrostomy tube and that the distance between the two esophageal stomas is short so that they could be readily joined by a skin tube.

The direct operation with extrapleural closure of the fistula and simultaneous primary anastomosis of the esophageal segments is favored by Shaw (14) Samson Lanman and the authors. provided the anomaly is such that an anastomosis is possible. Our experience in a small number of cases suggests that this type of operation can be done in most instances. The first reported operation of this type was described by Shaw (14) in 1939, who also quotes a personal communication from

Samson describing a case in which the same technique was employed. Lanman, in 1940, subsequently has reported 4 patients operated on by this technique in 1936 and 1937. It is believed that the first of Lanman's cases represents the first application of the principle of extrapleural closure of the fistula combined with primary anastomosis of the two segments of the esophagus. Although all of these patients died unfortunate circumstances contributed to the death of 2 of the patients. In one of Lanman's patients who lived 9 days postmortem examination suggested that death was due solely to overhydration with fluids administered by a continuous intravenous infusion. There was no leakage of the anastomosis, and cultures of the wound showed no growth. Shaw's patient died of a transfusion reaction on the 15th postoperative day. The esophageal anastomosis had been made over a No 8 F catheter. Postmortem examination showed that the anastomosed esophageal segments had separated for a distance of 13 millimeters, and the catheter could be seen lying in a nonepithelized tract consisting of granulation tissue. The esophageal opening into the trachea was closed and the stump was buried in granulation tissue. There was an extensive bilateral pneumonia, and two broncholeatic abscesses were present in the left lower lobe.

In a recent personal communication Shaw (15) mentions a successful case of reconstruction of the esophagus by the direct operation. The patient, who was 7 months of age at the time of Shaw's communication, was operated upon subsequent to the patient presented in this article. Shaw performed a gastrostomy on the 5th day following correction of the anomaly as difficulties were encountered in feeding the patient by mouth. The gastrostomy also allowed retrograde dilatations of the esophagus to be done at frequent intervals.

Our interest in the direct method of attack was stimulated by a personal communication from Shaw (13) in 1938 describing his first case. Prior to our knowledge of this case 3 patients had been operated on in this hospital. In 2 a gastrostomy was performed and in the 3d case the cardiac portion of the stomach was ligated and a gastrostomy was made. A

4th case, a premature infant, was not operated upon, as the patient died 27 hours after birth, and diagnosis was not made until postmortem.

In the period of  $3\frac{1}{2}$  years since Shaw's communication in 1938, 11 patients have been admitted to the University of Michigan Hospital with congenital atresia of the esophagus, a tracheoesophageal fistula being present in all except possibly 1 case. Two patients were not operated on because of prematurity and poor general condition, and both patients died within 24 hours after admission. In 7 of the 9 remaining cases, for whom an intrathoracic exploration was performed, operation was done with the intention of establishing continuity of the esophagus. Ligation of the fistula and an anastomosis of the esophageal segments were accomplished in 5 cases, and was successful in 1 case. The 2 cases for which an anastomosis was not contemplated are as follows: (1) the extrapleural operation in Case 7 was limited to ligation of the fistulous communication, and a gastrostomy was done for feeding. The anatomical findings, i.e., a normal size lower segment with an overlap of the two segments, were ideal for the performance of an anastomosis, but it was not attempted because of the discouragement resulting from the death of the 2 preceding cases in which an anastomosis had been done, (2) a gastrostomy was done in Case 15 as no air was present in the stomach. The gastrostomy feedings were regurgitated into the trachea, thereby demonstrating the patency of the lower segment. An extrapleural exploration of the anomaly was undertaken. The diameter of the contracted lower segment was too narrow to permit an anastomosis to be made, and the lower segment was ligated. We now believe that an extrapleural operation should be done as the primary operation, even when air is not present in the stomach, as an exploratory operation furnishes the deciding information that is necessary to determine whether an anastomosis is possible or whether the distal segment should be ligated and a gastrostomy done. The findings and method of treatment of the 15 cases observed in this hospital are charted in Table I. The result in all cases has been fatal except in the one described in detail in this report.

*Anesthesia* Provision should be made in advance of operation for the administration of positive pressure by the anesthetic gases or oxygen in the event that the pleural cavity is inadvertently opened. A face mask of sufficiently small size to fit air-tight over the infant's mouth and nose should be available for this purpose. Local anesthesia with  $\frac{1}{4}$  per cent metycaine hydrochloride is used until separation of the parietal pleura is begun, when light ether anesthesia by the drop method is started. If the extrapleural separation is done under local anesthesia, the straining of the infant may cause a tear of the parietal pleura by forcing it against the exposed ends of the ribs laterally. Quiet breathing obtained by general anesthesia enables the exposure of the mediastinum with an illuminated, spatula type of retractor to be maintained more easily than when local anesthesia alone is used. The absence of crying and straining is essential in allowing the anastomosis to be made satisfactorily. The advantage of ether anesthesia is particularly well illustrated in the case described in this article. During an attempt to perform the anastomosis under local anesthesia, the two esophageal ends were pulled widely apart whenever the infant strained or attempted to swallow. After satisfactory relaxation had been obtained with ether anesthesia, the esophageal ends were readily approximated without tension upon the suture line.

*Technique* The patient is placed in the lateral position and securely strapped to a frame. Heat is applied with hot water bottles to prevent chilling. A left vertical parascapular incision is made from the level of the second to the seventh ribs. Hemostasis is carefully obtained, as a small total amount of blood loss is relatively great for a newborn infant. The trapezius and rhomboideus major muscles are incised, and the sacrospinalis muscle is retracted mesially. In our earlier cases, short lengths (1 to 2 cm.) of the second to sixth ribs inclusive were resected adjacent to their transverse processes, which were shortened. A perforation of the parietal pleura occurred in at least 1 and possibly 2 cases due to the parietal pleura being forced against the lateral ends of the ribs during straining, and in spite

TABLE I—ANALYSIS OF 15 CASES

Case No.	Opera-tion after birth	Died after operation	Operation	As in stomach before operation	Perforation during operation	Adhesions favorable for future success	Remarks
Case 1. B. G. F. 1922	days	Yes	Contrast study	Yes	—	Yes	Fracture (3 mm) Aspiration per- formed
Case 2. R. B. 1926	days	3 hrs.	Contrast study and laparotomy of cardiac end of esophagus	Yes	—	Yes	Aspiration performed. Adhesions
Case 3. B. B. C. 1927	days	2 1/2 days	Laparotomy	Yes	—	Yes	Fracture (2-3", mm) Aspiration performed
Case 4. B. B. S. 1927	No opera- tion	27 days after birth	None	No (2-3")	—	Yes	Fracture 7 1/2 mm. Adhesions of stomach not diagnosed until autopsy
Case 5. R. M. O. 1929	days	Yes	Left retroperitoneal section of stomach. Anastomosis of esophageal segment over T-tube	Yes	Yes	Yes	Upper esophageal segment adherent to and perforated lower segment. Death due to shock
Case 6. C. A. B. 1929	days	Dead during operation	Right retroperitoneal laparotomy of stomach. Anastomosis of esophageal segment over T-tube	Yes	Yes (no aspiration)	Yes	Emphysema because progressively more shallow and shallow after pleural cavity was opened
Case 7. O. F. 1929	12 days	days	Left retroperitoneal laparotomy of stomach. Anastomosis and aspiration	Yes	No	Yes	Upper esophageal segment adherent to and perforated lower segment. Death due to emphysema
Case 8. M. W. 1929	days	Dead due to operation	Right retroperitoneal laparotomy Cecum segment not found	Yes	Yes	No	Operation complicated by bilateral pneu- mothorax and injury to aorta
Case 9. F. C. 1931	4 1/2 days	days	Left retroperitoneal laparotomy of stomach. Anastomosis over catheter. Partial pleurotomy, resulting in slight drainage of pleural cavity	Yes	Yes	Yes	Opening of esophageal segment proved at operation. Death due to sepsis
Case 10. J. M. J. 1932 Re- ported in detail	12 days	Living	Left retroperitoneal laparotomy of stomach. Anastomosis of esophageal segment	Yes	Yes	Yes	Patent living 3 1/2 mm. after operation
Case 11. O. W. 1932	No opera- tion	Dead, days after birth, day after admission	None	Yes	No opera- tion	No Autopsy	Adhesions present on admission. Condi- tion too poor to permit operation. As- sumed of esophagus and air in stomach on x-ray examination. Premature
Case 12. R. B. 1932	6 days	12 hrs.	Left retroperitoneal laparotomy of stomach. Anastomosis of esophageal segment	No	No	No	No air in stomach. Abnormally small distal segment arising from right lung bronchus, extending to peritoneal cavity on left below bifurcation of trachea. (Open thoracotomy) Stomach fused at operation. Anastomosis intact at autopsy. Cerebral pneumonia and shock.
Case 13. K. M. 1932	days	8 days	Left retroperitoneal laparotomy. Anastomosis and possible anastomosis of constricted lower segment	Yes	No (distal)	No	Abnormally small distal segment arising from trachea. Operation terminated without laparotomy of distal segment be- cause of poor condition. Death due to hemorrhage from tissue infarction of lower end of esophagus
Case 14. J. T. 1932	No opera- tion	Dead 6 days after birth, day after admission	None	No	No opera- tion	No Autopsy	Poor condition of patient prevented operation. Premature
Case 15. F. G. 1932	Contrast study 6 days after birth. La- parotomy of stomach 15 days af- ter birth	Dead days after operation of stomach	Contrast study because of admission of air in stomach. Subsequent left retroperitoneal laparotomy of stomach because of stricture of gastric fundus	No	No	No	Lapotomy of stomach delayed until 15 days after birth because of adhesions fol- lowing gastroenterostomy. Anastomosis not attempted because of abnormally small distal segment. Death due to pneu- mothorax from infarction of esophagus from air in stomach

(\*) Questions by Dr. Frederick A. Collins.

(†) Question by Dr Henry E. Lamm.

Operation by Dr. John Alexander

H5 The autopsy protocols in Cases 1-4 do not mention the diameter of the lower segment.

[illegible]

surviving patients, linkage of the chromosome has occurred previously. In all of the patients, surviving 30 months, the chromosome was not subsequently removed on the postoperative day. Primary healing of the wound occurred, but subsequent linkage at the site of the anastomosis resulted in the redevelopment of tracheo-oesophageal fistula. Each still present in the patient was living 30 months, tracheo-oesophageal fistula, subsequent to the anastomosis, was not observed. In each case, the patient died of a cause unrelated to the anastomosis. The patient who died of a cause unrelated to the anastomosis had been mistakenly diagnosed in the first breast case, and appears to give better support of the dual oesophageal argument than does the left intrathoracic approach.

of the fact that the rib ends had been made smooth in order to lessen the chance of this complication. We now resect longer lengths (4 to 5 cm) of the second to fifth ribs inclusive, removing the ribs back to their transverse processes. In the last 5 cases perforation of the pleura has occurred in only 1 case. The importance of avoiding an opening of the parietal pleura cannot be overstressed. In the one patient for whom an intrapleural operation was intentionally done, and in another patient in whom the parietal pleura was torn during operation, the complication of a pneumothorax, even though controlled by positive pressure, added greatly to the respiratory embarrassment during the operation and was a contributory cause of death. An opening of the parietal pleura is particularly serious in infants because the respiratory reserve is only slightly greater than the tidal air requirements. In another patient in whom the parietal pleura was torn during operation, air-tight drainage of the pleural cavity was required at the conclusion of the operation because the pleural rent could not be satisfactorily sutured.

The intercostal muscles and nerves are next divided and the intercostal vessels are doubly ligated and divided. As the parietal pleura can be injured easily during this part of the operation, the periosteum is incised vertically after it has been separated from the parietal pleura. The extrapleural separation is carried out slowly with a small blunt dissector. An illuminated retractor is useful in maintaining the exposure. The parietal pleura is freed out of the costovertebral gutter until the posterior mediastinum is reached. One or more branches of the highest intercostal vein may need to be ligated and divided in order to expose the posterior mediastinum. The left subclavian artery is retracted forward and to the right by the illuminated retractor.

The blind upper end of the esophagus is usually readily found in the upper portion of the posterior mediastinum. It is recognized by the distinctive color and the vertical direction of its external musculature. The diameter of the upper segment is usually about 1.5 centimeters. If the upper segment is not identified promptly, a catheter should be introduced by mouth and advanced until

the upper segment can be recognized by palpation of the catheter within it. If the upper segment does not extend down to the level of the operative field, pressure can be made upon the catheter, thereby pushing the upper segment down to a level where it can be found. The tip of the upper segment is secured with a tension suture.

The identification of the lower segment is often more difficult than the identification of the upper segment. In order to gain adequate exposure of the lower segment, the upper one or two intercostal arteries arising from the aorta should be doubly ligated and divided in order to allow the arch of the aorta to be displaced forward and downward. The lower portion of the trachea is identified by palpation of the tracheal cartilages. The diameter of the lower segment, unless contracted, is usually about 6 millimeters or approximately one-half the diameter of the upper segment. When the lower segment arises from the trachea at a distance of 1 to 1.5 centimeters above the carina, recognition of the lower segment is accomplished without difficulty. The longitudinal musculature of the esophagus again aids in identification, although the membranous posterior wall of the trachea possesses a similar appearance which may be misleading.

The separation of the lower segment from the trachea is begun at a point about 1 centimeter below the fistulous communication. A right-angled hemostat with a blunt tip is a convenient instrument for this purpose. The anterior wall of the lower segment is more firmly attached to the posterior wall of the trachea than is the case with the upper segment. The cleavage plane between the lower segment and the trachea may be difficult to develop, although in our cases it has always been possible to do so by blunt dissection. As soon as the instrument has been passed completely around the lower segment, a tape is placed around it in order to provide tension, so that the dissection can then be carried upward to the fistulous communication. The diameter of the lower segment should be carefully estimated. A very narrow lower segment (3 to 4 mm) may require that an anastomosis should not be attempted, but that the fistula

should be ligated. A gastrostomy and cervical esophagostomy would then be performed at subsequent operations. In our cases a contracted lower segment has been a greater obstacle to the performance of an anastomosis than has the distance of separation of the two segments.

Closure of the fistula is most readily accomplished by a single silk ligature placed around the esophagus and tied as close to the trachea as possible. In one case the lower segment was incised almost flush with the trachea, and the fistulous communication was closed with interrupted sutures of plastic silk. An air tight closure was not obtained and the closure was a more difficult procedure than when a single ligature had been used. A tension suture is placed in the wall of the distal segment which is then divided close to the ligature. The lumen is cleaned with a mild antiseptic solution. Packing off of the operative wound with gauze has not proved satisfactory because of the limited exposure. The tension suture in the wall of the upper esophagus is held taut and the blind end is opened to approximately the same diameter as that of the lower segment.

The anastomosis is usually constructed in two layers with interrupted sutures of plastic silk on baby Emmet needles. Approximately 6 or 7 sutures that include all coats of the esophagus are placed in the first row. A second layer of inverting sutures includes only the muscularis and the submucosa. The anastomosis was made over a small T tube in 2 of our cases. In another case the anastomosis was made over a catheter introduced through the wound, one end being advanced into the upper segment and brought out through the mouth, and the other end advanced into the stomach. When a T tube is used, the anastomosis is constructed with more difficulty than without the tube. The anastomosis, however, is more readily done over a catheter than without one. If a catheter is used, it is removed after the anastomosis has been completed, as the presence of a catheter in the esophagus following operation not only causes an increased stimulation of pharyngeal secretions, but also tends to obstruct the esophagus at the site of the anasto-

mosis, thereby allowing the secretions that collect in the upper esophageal segment to spill over into the trachea. Furthermore it is believed that healing is more satisfactory if a foreign body is not present within the esophageal lumen. A small soft rubber drain is placed in the lower angle of the incision and advanced to the region of the anastomosis, so as to afford drainage in the event that leakage should occur. Closure of the wound is begun by approximating the anterior ends of the intercostal muscles to the under surface of the sacrospinalis muscle. The extracostal wound is closed in layers, the closure being made securely around the drain to prevent the sucking of air into the extrapleural space. The chest should be examined immediately following operation to be certain that a pneumothorax has not resulted from an unrecognized opening in the parietal pleura.

#### POSTOPERATIVE CONSIDERATIONS

The infant should be kept in a prone position to prevent the gravitation of oral and pharyngeal secretions into the trachea. Elevation of the foot of the bed is desirable for the same reason and also as a measure to counteract operative shock. The body temperature should be recorded immediately after operation. Heat is applied if the temperature is subnormal. A continuous flow of oxygen administered by a tent is routinely employed. Supplementary inhalations of 5 per cent carbon-dioxide and 95 per cent oxygen are used to increase pulmonary ventilation. A blood transfusion is not given immediately after operation unless it is urgently required as it is preferable that the infant should not be further disturbed by a transfusion until a period of a day or more has elapsed. Codeine in frequent small doses is advisable to keep the infant quiet and to prevent tension being placed upon the anastomosis by crying and straining. Sulfonamide therapy is continued as a prophylactic measure and a suitable ascorbic acid blood level is maintained by daily injections.

Fluids consisting principally of 5 per cent dextrose are administered by subcutaneous infusion. Care should be exercised to prevent overhydration and the amount of fluids

should be considerably less than that ordinarily given to a normal infant. Intravenous fluids, unless given in small quantities, tend to cause pulmonary edema and are best avoided. A transfusion of whole blood or plasma should be given as a supportive measure when indicated to prevent the depletion of serum proteins that otherwise would occur. The use of parenteral fluids is continued until an adequate formula can be given by mouth or until it is ascertained that a gastrostomy will be needed because of leakage. Unless there is evidence of leakage, fluids can be started by mouth several days after operation. The feedings should consist at first of a few drops of 5 per cent glucose. If this is tolerated without choking, the amount is rapidly increased to 2 to 4 cubic centimeters at each feeding. A diluted formula of similar amount is then begun, and the feedings are given slowly with a Breck feeder. The amount of the formula, and later its consistency, are constantly increased until a normal formula can be given.

Röntgen examination of the esophagus should precede the administration of fluids by mouth. The initial examination is conveniently carried out with a portable unit and should consist of a roentgenogram made immediately after the administration of a few drops of lipiodol by mouth. Fluoroscopic examination is more important than film studies in determining the condition of the anastomosis, but a fluoroscopic examination should not be undertaken until the infant's general condition permits it to be done safely. As the crying and struggling of the infant during a fluoroscopic examination place tension upon the anastomosis, the initial fluoroscopy should preferably not be attempted until 10 or 12 days after operation. Interval fluoroscopic examinations are particularly indicated in the subsequent management of the case, so as to determine if a probable stricture at the site of the anastomosis will require dilatation.

Should a gastrostomy be elected, it is preferable to defer the operation until a period of at least 4 or 5 days has elapsed after closure of the fistula, to allow the infant to recover from the effects of the first operation. In 1 of

our cases, in which the tracheoesophageal fistula was ligated and no attempt was made to perform an anastomosis, a gastrostomy was done immediately at the conclusion of the extrapleural operation. We realize now that the performance of the gastrostomy immediately after the extrapleural operation was inadvisable as it subjected the patient to an unnecessary amount of surgery at one time. The extrapleural drain should not be removed until it is evident that there is no leakage at the site of the anastomosis.

An important cause of death in patients with congenital atresia of the esophagus is bronchopneumonia resulting from a spillover of pharyngeal secretions into the tracheobronchial tree. Accordingly, efforts should be directed toward maintaining the pharynx and tracheobronchial tree constantly free of secretions, and frequent observations should be made to detect the presence of secretions as soon as they occur. Particular attention should be paid to the character of the respirations by listening with a stethoscope placed close to the patient's mouth. Intermittent pharyngeal suction is indicated as soon as pharyngeal secretions are evident. The onset of bronchial secretions is first recognized by the presence of rhonchi and wheezes. When the physical signs of bronchial secretions are noted in one lung, hyperventilation with carbon dioxide-oxygen inhalations should be administered with the patient lying on the contralateral side. Should the secretions persist, an effort should be made to dislodge them by crying or by coughing, the latter being induced by the application of pharyngeal suction with an aspirating catheter. In the event that bronchial secretions cannot be cleared by these measures, bronchoscopy may be needed for aspiration of the secretions. As an early atelectasis or bronchopneumonia may escape clinical recognition, the chest should also be examined by roentgenograms at daily intervals during the first several postoperative days. Furthermore, a pleural effusion of sufficient amount to require thoracentesis may occur on the operative side as a result of the extrapleural operation. The amount of the fluid can best be determined by roentgenograms.



## SUMMARY

The surgically ideal plan for the correction of congenital atresia of the esophagus with tracheoesophageal fistula is a reconstruction of the continuity of the esophagus by an extrapleural ligation of the fistula and an end-to-end anastomosis of the esophageal segments. The first successful case of reconstruction of the esophagus by this plan is presented. The factors pertaining to operative correction of the anomaly and experiences in a series of 15 cases are discussed.

## REFERENCES

- CARTER, B. N. *Surg. Gyn. Obst.*, 94: 78-89-90.
1. GAGE, M., and OCHSNER, A. *Ann. Surg.* 93: 3-737.
2. GARDNER, H. A. *Ann. Surg.* 93: 107-70-707.
3. HEATH, C. A. *Ann. Otol. Rhin. & Laryng.*, 15: 45-2-3.
4. LAMM, T. H. *Arch. Surg.* 94: 4-96-1-13.
5. LEVY, A. L. *J. Thoracic Surg.* 9: 6-30-30.
6. *Ibid.* 94: 645-657.
7. MERRILL, C. G. Discussion of article by Gage and Ochsner.
8. RICHTER, H. M. *Surg. Gyn. Obst.* 9: 2-39-402.
9. ROBERTSON, A. H., and HINCKLEY, U. *Arch. Ped.* 93: 49-448-452.
10. SAMMON, P. C. Quoted by Shaw.
11. SCOTT, W. J. M. Quoted by Heath.
12. SHAW, R. C. Personal communication to Dr. John Alexander October 2, 1918.
13. *Ibid.* *J. Thoracic Surg.* 9: 90-91-3-112.
14. *Ibid.* Personal communication, February 9, 1919.
15. STARR, E. D. *Ann. J. Surg.* 9: 3, 571-57-553.
16. TUCKER, G., and FROEDIGER, E. P. *J. Am. M. Ass.* 93: 10-326-137.
17. VOLT, E. C. *Ann. J. Roentgenol.* 9: 23-465-466.

# TRAUMATIC PERITONITIS CHOICE OF ROUTES FOR ADMINISTRATION OF SULFONAMIDES

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**I**N World War I, the mortality rate (10) in patients reaching the operating room with a perforation of an abdominal viscus was 50 per cent or more. Early deaths were due to hemorrhage and shock. In those dying a few hours later, peritonitis played a major rôle.

During the past few years a marked change has taken place in the treatment of infections, namely, the use of chemotherapy in the form of sulfonamide drugs. In pneumonia, the frequency of parenteral sulfonamide dosage necessary to maintain adequate blood concentration is well understood. While most surgeons use one or another of the sulfonamide drugs when dealing with a potential peritoneal contamination or an established peritonitis, it seems to us that the attainment of an adequate concentration over a period of time is not clearly understood. Certainly with the necessity for treating a great number of perforating injuries of the abdomen in war, the several methods for rapid establishment of an adequate intraperitoneal concentration of one of these drugs, and of equal importance, the necessity of maintaining it, should be understood by all.

Saduck, Black, and Seymour gave 4 grams (0.06 per kilogram) of sulfathiazole per os to adults and found that the maximum concentration in the blood was reached after 3 hours and that it had fallen off greatly after 6 hours. Haag and his co-workers have shown that in dogs it takes 2 to 4 hours to reach maximum blood concentration after oral administration of sulfanilamide, sulfathiazole, and sulfapyridine, and this level is maintained for 2 to 4 hours. With a dose of 100 milligrams per kilogram of sulfathiazole, on an empty

stomach and without peritonitis, they found that the blood concentration reached 4 milligrams per cent after 3 hours and maintained this level for 3 hours before falling. This dose would be equivalent to 6.8 grams in a 150 pound man. Long advises the oral administration of 2 to 4 grams of sulfanilamide at the time of an injury. We understand that the Army recommends 6 grams by mouth.

In early peritonitis, we shall show the time necessary to establish adequate blood and intraperitoneal concentration of various sulfonamides after administration by mouth, intravenous injection, implantation of crystals into the abdomen, and injection of sulfonamides intraperitoneally. In our experiments we produced peritonitis in 75 dogs, 716 determinations of sulfonamide concentrations in heart blood and peritoneal fluid were made.

Sulfanilamide by mouth in early peritonitis did not produce adequate blood and peritoneal fluid concentrations in dogs. Under sodium nembutal anesthesia, we made a 1 centimeter transverse incision in the colon of dogs and dropped the bowel back into the peritoneal cavity. This was done in 3 animals. One hour later by gavage we gave sulfanilamide equal to a human dose of 6.5 grams to 2 dogs and to 20 grams to 1 animal (Fig 1, slide 48). The maximum peritoneal fluid concentration was not reached until 2 to 4 hours later and then it was inadequate.

Common practice is to pour sulfanilamide, sulfathiazole, or other sulfonamide powders into the abdomen at the time of operation for perforation. In war, this is apt to be many hours after the injury. The following experiments were made to determine the best way to establish an early, high sulfonamide level in the peritoneum before peritonitis is established—preferably done at the first dressing station.

From the Surgical Service, Presbyterian Hospital and the University of Illinois College of Medicine.



Fig. 1. Slide 43, dog, weight 6 pounds. Colon injury at 9:00 a.m. Sulfanilamide, .95 gram, given by gavage 1:00 p.m. Colon injury closed at 2:30 p.m. Graph shows the concentration found after the drug was given.

Within 15 to 30 minutes after solutions of sodium sulfathiazole are given rapidly by vein we found that there will be a high concentration in the exudate of an early peritonitis. This was determined by the following experiments.

A short incision was made in the midline of the dog's abdomen. The colon was identified and an incision 1 centimeter long was made transversely through all layers of the colon. We did not attempt to prevent contamination with feces. The open bowel was dropped back into the abdominal cavity and the abdominal wall was tightly closed with interrupted through-and-through sutures. All blood for sulfonamide determination was drawn from the heart by puncture with a long needle. Peritoneal fluid was aspirated by inserting a sterile glass catheter between the stitches. An aseptic syringe supplied the suction. The time of administration and withdrawal of all drugs and samples was noted. Fifteen minutes to 1 hour after the abdomen was closed a 10 per

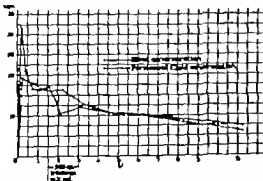


Fig. 2. Slide 59, dog, weight 28 pounds. Fifty cubic centimeters of 10 per cent turpentine emulsion as injected into the peritoneum 9:30 a.m. Sodium sulfathiazole, .4 grams in 14 cubic centimeters of sterile water was given by vein at 9:40 a.m.



Fig. 3. Slide 6, dog, weight 30 pounds. Colon injury at 9:30 a.m. Sodium sulfathiazole, .5 gram in 10 cubic centimeters of sterile water given by vein at 9:45 a.m. Colon injury closed at 1:00 noon.

cent solution of sodium sulfathiazole .5 gram per 10 pounds weight, was given intravenously, rapidly. The colon injury was closed 3 to 4 hours later.

In 6 animals, therapeutic concentrations in blood and peritoneal exudate were present  $\frac{1}{2}$  hour after administration by vein. Therapeutic concentrations were maintained for 3 $\frac{1}{2}$  hours in spite of dilution by 500 cubic centimeters of physiological salt solution given by vein over a 4 hour period starting  $\frac{1}{2}$  hour after the drug was given (Fig. 2 slide 61).

In 12 other animals, the same procedure was followed except that no fluid was given by vein. Fewer determinations were made. The same therapeutic levels were reached but they seemed to fall less rapidly.

In order to determine the effect of a strong irritant on peritoneal sulfonamide concentration, we injected 20 cubic centimeters of 25 per cent turpentine emulsion into the peritoneal cavity through a hypodermic needle in 3 dogs. No colon injury was made. Fifteen minutes after the turpentine was injected, a 10 per cent solution of sodium sulfathiazole .5 gram per 10 pounds, was rapidly injected by vein. Fifteen minutes after the administration of the drug the concentration in the peritoneal exudate was 19 to 22 milligrams per cent in each animal (Fig. 3 slide 59). These animals were given intravenous physiological salt solution.

These experiments show that during a rapid outpouring of peritoneal exudate if the blood concentration of sulfonamide is high, the concentration in the peritoneal fluid can be raised to therapeutic levels within 15 minutes.

We have found that as the blood level fell the peritoneal concentration lagged. The peritoneal fluid apparently acted as a reservoir

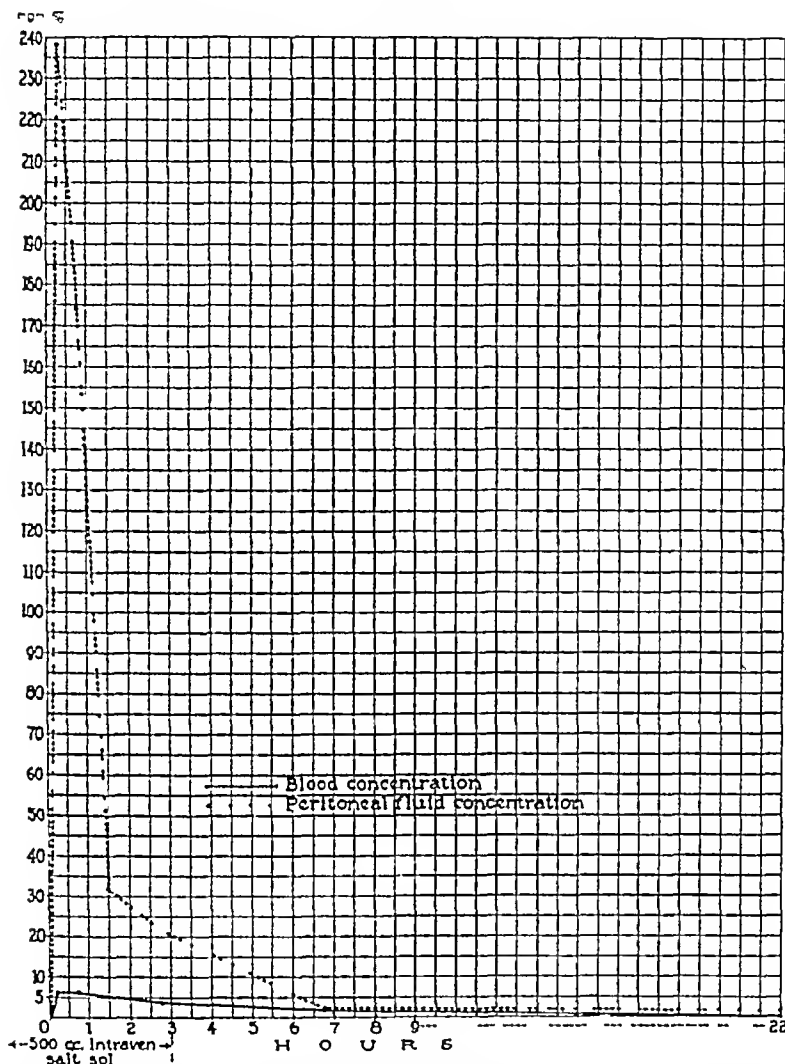


Fig. 4 Slide 41, dog, weight 17 pounds Colon injury at 9 15 a m Sodium sulfathiazole crystals, 0.85 gram, placed in the abdomen when colon injury was closed at 1 45 p m

This corroborated the findings of Gregory, in pleural and ascitic fluids

Similar experiments in dogs, in which the same dosage of intravenous sodium sulfadiazine were used, showed toxic injuries to the animals. This merits further study.

There is great difference of opinion as to the effect of placing various powdered or crystalline sulfonamides in the peritoneal cavity. Jackson and Collier found that there are fewer adhesions in experimental peritonitis after

sulfanilamide crystals have been placed in the abdomen. Other authors have given contrary reports. Throckmorton says that in rats crystals placed intraperitoneally give an increasing cellular reaction in the following order: sulfanilamide, sulfathiazole, and sulfapyridine. They saw no severe reaction with any one. Sulfathiazole evidently took 3 to 5 days to absorb. Ryan and his co-workers say that sulfadiazine is more slowly absorbed than sulfanilamide. Ambrose and Haag found

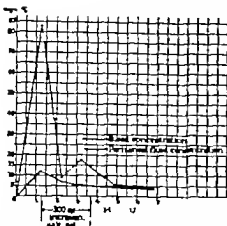


Fig. 5. Slide 55, dog, weight 8 pounds. Colon injury at 9:00 a.m. Sodium sulfathiazole, 8 grams in 80 cubic centimeters of sterile water was injected into the peritoneal cavity by needle and syringe at 4:15 a.m.

that in the normal peritoneum 100 milligrams of crystals per kilogram placed intraperitoneally gave blood levels after 2 hours of sulfanilamide 8 milligrams per cent—this dropped after 3 hours, sulfathiazole 4 milligrams per cent—this dropped after 4 hours and sulfapyridine 2.5 milligrams per cent—this dropped after 7 hours. Shumacker and Haag and Spelman found similar results.

We found that soluble sulfonamide crystals placed in the abdomen in early peritonitis produces a high, immediate concentration in the peritoneal exudate. The blood concentration rapidly reaches therapeutic levels, but falls after 2 to 4 hours. This was shown in the following manner:

In 6 dogs, colon injuries were made as described previously. After 2 to 5 hours, laparotomy was performed the injury closed, and 0.5 gram of sodium sulfathiazole crystals per 10 pounds weight was placed in the abdomen (Fig. 4, slide 41). After 15 minutes, the concentration in the heart blood was 6 milligrams per cent. The peritoneal concentration fell to 3.1 milligrams per cent after 2 1/4 hours, and at that time the blood concentration was 4 milligrams per cent. During this time the animals received normal salt solution intravenously. In these 6 animals, the highest peritoneal concentration was 1.42 milligrams per cent and that animal had a maximum blood concentration of 14 milligrams per cent.

The blood concentration remained above 10 milligrams per cent for only 2 hours. In the 5 others, the blood concentration did not go above 10 milligrams per cent and usually it was much below. All of these animals received intravenous salt solution immediately after closure of the injury.

In 2 other animals we used sulfanilamide crystals comparable to an 8 and 12 gram dose in an adult. The maximum blood concentration did not go above 10.6 milligrams per cent. The peritoneal concentrations of sulfanilamide were 834 milligrams per cent and 1,379 milligrams per cent after 1 hour. These dogs also received intravenous fluid after operation.

When soluble sulfonamides are placed intraperitoneally in an early peritonitis, there is a rapid elevation of blood concentration approaching therapeutic levels. This falls below 5 milligrams per cent after 2 to 4 hours. When intravenous sulfonamide has been given in the preceding 6 hours, care must be exercised to avoid summation of dosage if soluble crystals are later used intraperitoneally.

There is one other quick method of obtaining an adequate intraperitoneal concentration of one of the sulfonamides. This is the injection of suspensions or solutions through the abdominal wall or wound of entrance. It can be done with little danger. Ordinary care should prevent the injection of the fluid into a viscus. We made colon injuries in 4 dogs, and 3 hours later injected solutions of sodium sulfathiazole into the peritoneal cavity by needle and syringe. In 2 animals we injected 0.5 gram of sodium sulfathiazole per 10 pounds body weight. With both a 1 per cent and a 10 per cent solution, therapeutic concentrations were maintained in the blood for 3 1/2 hours and in the peritoneal fluid for 4 1/2 hours (Fig. 5 slide 55).

In 2 other animals the same procedure was carried out with 5 per cent solution of sodium sulfathiazole 1 gram per 10 pounds body weight. This is double our usual dose. In both animals the blood concentration was 33 milligrams per cent after one hour (Fig. 6 slide 46). Therapeutic levels were maintained for 7 hours in both blood and peritoneal fluid.

If a solution of sodium sulfathiazole is injected into the peritoneal cavity before opera-

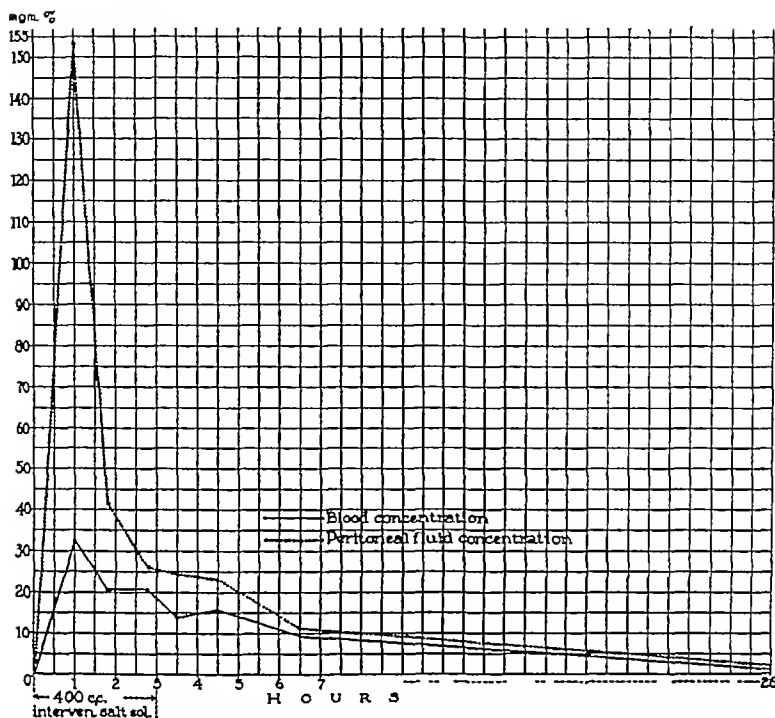


Fig 6 Slide 46, dog, weight 15 pounds Colon injury at 9 20 a.m Sodium sul fathiazole, 1 5 grams in 30 cubic centimeters of sterile water, was injected into the peritoneal cavity by needle and syringe at 12 noon

tion for traumatic peritonitis, an immediate high concentration is obtained. The blood and peritoneal fluid concentrations fall below therapeutic levels after 3 to 4 hours if the usual dose is used. If the dose is doubled, the blood concentration is high for 3 to 6 hours, and the intraperitoneal concentration maintains therapeutic levels for 7 hours.

We have shown that soluble sulfonamides placed intraperitoneally in early peritonitis result in a rapid elevation of blood and peritoneal concentration and a rapid fall in concentration after  $3\frac{1}{2}$  hours. We have found that the less soluble sulfathiazole crystals placed intraperitoneally produce an immediate high concentration in the exudate. This level is maintained for 24 to 48 hours. Many samples of exudate still have visible crystals at 48 hours. When the exudate was centrifuged, the concentration of sulfathiazole in the supernatant fluid remained high for at least 4 hours, but the concentrations were less than those found in the same fluids before centrifuging.

We are not able to state whether the presence of undissolved crystals in the free fluid exerts any bacteriostatic effect. The blood concentration slowly rises to a peak 4 to 8 hours after administration. It usually remains below therapeutic levels.

In 5 dogs we placed 0.5 gram of sulfathiazole crystals per 10 pounds weight, intraperitoneally when closing a 2 to 4 hour colon injury (Fig 7, slide 72). In 1 animal the blood concentration gradually rose to 10.4 milligrams per cent during 8 hours. In another it rose to 7.8 milligrams per cent in 8 hours. The 3 dogs remaining had blood concentrations of 0.9 milligram per cent to 4.7 milligrams per cent, the rise occurring in the same manner.

In another 3 dogs, a commercial preparation of finely divided crystals of sulfathiazole held in suspension was used (Fig 8, slide 73). In 1, the suspension was injected intraperitoneally through the abdominal wall by syringe and needle 1 hour after the colon injury. In another, the suspension was injected through a

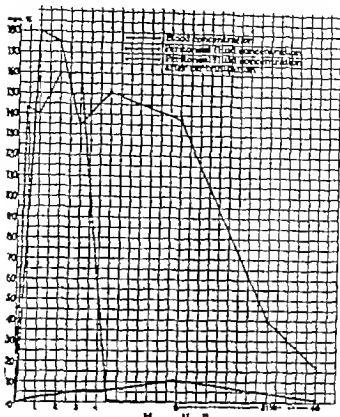


Fig. 7. Slide 72, dog, weight 10 pounds. Colon injury at 9:35 a. m. Sulfathiazole crystals, 0.5 gram, were placed in the abdomen when the injury was closed at 12 p. m.

catheter pushed through the wound of entrance 1 hour after colon injury. In the third the suspension was placed in the abdomen at the time of closure of the injury. In the first 2 the colon injury was closed 2 hours after the suspension was injected. The blood concentrations rose to about 5 milligrams per cent after 2 hours, and tended to maintain this level for 6 to 8 hours. The peritoneal concentrations resembled those seen with ordinary crystals.

All animals receiving intraperitoneal sulfathiazole crystals did well and when killed after 2 to 9 days very few adhesions were found.

As a control, the same dose of sulfathiazole crystals was inserted through a laparotomy incision without bowel injury. Examination 4 days later showed no peritoneal reaction and no fluid present. Sulfathiazole crystals were

found free in the abdomen. Walter and Cole in an abstract of an unpublished report used sulfadiazine in the abdomen. Six to 7 days were required for complete absorption. The blood level reached a peak in 36 and 96 hours.

In another animal a suspension of microcrystals was injected by needle without laparotomy. Five days later examination showed no trace of peritoneal reaction. None of the injected material was found.

The use of this less soluble sulfonamide as an intraperitoneal drug will lessen the danger of summation with previously administered intravenous drug.

We have some human material in which the findings correspond to the results found in our experiments. A 30 year old male who had a 20 hour attack of acute appendicitis was operated upon and a diffuse purulent peritonitis

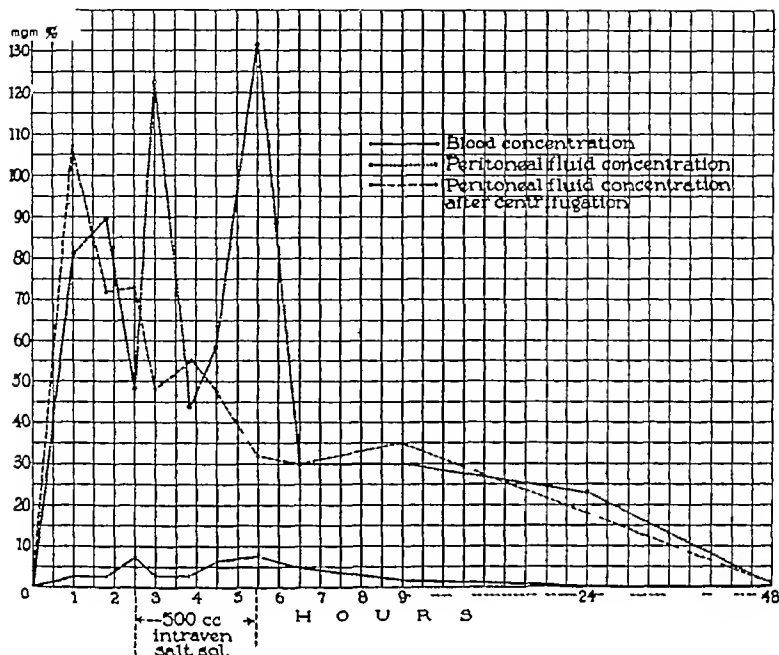


Fig 8 Slide 73, dog, weight 16 pounds Colon injury at 9 00 a.m Sulfathiazole microcrystals, 0.8 gram in 20 per cent suspension, was injected into the peritoneal cavity by needle and syringe at 9 55 a.m. Colon injury was closed at 12 30 p.m.

was found. The appendix was removed and 7.5 grams of sodium sulfathiazole in 125 cubic centimeters of normal saline was placed in the peritoneal cavity just before tight closure. The blood concentration of the sodium sulfathiazole was 6.8 milligrams per cent after 30 minutes and it was 6.5 milligrams per cent after 3½ hours. Only a trace was found after 10 hours. In 4 cases in which sulfanilamide was placed in the human abdomen at operation, comparable doses being used, blood concentrations were also found to be low after 8 hours.

A man who had a colostomy developed peritonitis. Ten grams of sulfanilamide was

placed in the peritoneal cavity around the colostomy. Five and one-half hours later, the blood level was 2.6 milligrams per cent. The next day he was given 5 grams of sodium sulfathiazole intravenously over a 3 hour period. One-half hour after the administration of the fluid and drug was stopped, the blood concentration was 9.5 milligrams per cent, but 12½ hours later, the blood concentration had fallen to 2.6 milligrams per cent.

A 48 year old man had a 3 day old generalized peritonitis following the giving of an enema which ruptured a diverticulitis. He was desperately ill (Fig 9, slide 51). An abdominal paracentesis was made and 450 cubic

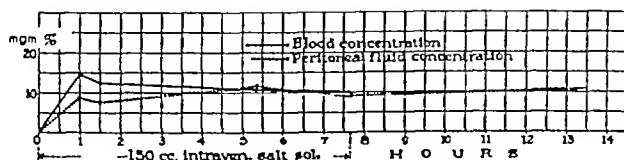


Fig 9 Slide 51 Man, weight 150 pounds, with 72 hour old peritonitis. Sodium sulfathiazole, 7.5 grams in 150 cubic centimeters of sterile water, was given intravenously, rapidly.



centimeters of cloudy fluid was aspirated. One and one-quarter hours later 7.5 grams of sodium sulfathiazole was given intravenously in a 5 per cent solution, rapidly. One hour later the blood concentration was 14.6 milligrams per cent and the peritoneal fluid aspirated through the paracentesis opening had a concentration of 8.3 milligrams per cent. This patient had large amounts of intravenous fluid and plasma, but 7½ hours after the injection the blood and peritoneal concentrations were 10 milligrams per cent. He died 5 hours after this. At postmortem, the peritoneal fluid contained a sulfathiazole concentration of 10.3 milligrams per cent. In animals, we have noticed a similar flatness of the curve when death approaches.

#### CONCLUSIONS

Sulfanilamide given by mouth after injury to the peritoneum will not produce adequate early concentrations in blood and peritoneal exudate. A 10 per cent solution of sodium sulfathiazole may be injected intravenously without producing phlebitis. Fifteen minutes after such an injection, the effective sulfathiazole level in the peritoneum will approach that found in the blood. Therapeutic concentration in the peritoneal fluid will be maintained for 4 to 6 hours. The fall in concentration will be hastened by giving intravenous fluid if circulation is adequate. When soluble forms of drug are used, an additional dose must be administered after 8 hours if therapeutic concentrations are to be maintained.

If sodium sulfathiazole solution is injected into the abdominal cavity after the injury is made and before closure of the perforation an immediate high concentration is obtained. The blood concentration rises to therapeutic levels rapidly and is maintained 4 to 6 hours. When sodium sulfathiazole or sulfanilamide crystals are placed in the abdomen at operation there is a rapid high concentration of drug in the peritoneal exudate. The blood concentration rises to therapeutic levels rapidly and falls below therapeutic levels after 6 hours.

Further study may show that other soluble sulfonamides are preferable to the sodium sulfathiazole used in our studies. When rela-

tively insoluble sulfathiazole crystals are placed in the abdomen effective concentrations are reached in the peritoneal exudate in 20 minutes. Effective concentrations of the drug are maintained in the peritoneal exudate for many hours. The concentration in the blood rises slowly and usually remains below therapeutic levels.

It is desirable to establish conditions unfavorable to bacterial growth within the abdomen as soon as practicable after injury. Such conditions should be maintained until the perforation is closed and the natural defenses of the peritoneum have dealt with the contaminating organisms.

A program for retarding the development of peritonitis after bowel perforation is suggested.

1. One-half gram of sodium sulfathiazole per 10 pounds body weight should be injected intravenously as a 5 or 10 per cent solution. This injection should take from 2 to 4 minutes and should be a first aid measure. Intravenous fluid, plasma, or blood should follow. As an alternate procedure a soluble drug or a suspension of sulfathiazole microcrystals may be injected directly through the abdominal wall or in some cases through the entry wound.

2. As soon as possible laparotomy should be performed. At that time a relatively insoluble sulfonamide such as sulfathiazole, should be placed in the abdomen. When soluble sulfonamides are used in the abdomen, additional drug must be administered after 8 hours. When slowly soluble sulfathiazole is used in the abdomen, additional drugs need not be administered for 24 hours.

#### REFERENCES

1. ALLEN, A. A., and HALL, H. B. *Surgery* 1945, 903.
2. GELBOY, R. Arch. J. C. M., 1945, 69, 470.
3. HALL, H. B., SPEARMAN, C. R., and MCCOY, H. M. *Surgery*, 1945, 572.
4. JACKSON, H. C., and COLLIER, F. C. *J. Am. M. Ass.* 1945, 131, 91.
5. LLOYD, PIERCE H. *J. Am. M. Ass.* 1945, 131, 303.
6. L. OYER, C. and BURBAUGH, C. *Surg. Gyn. Obst.* 1945, 74, 57.
7. R. A. D. BATHUR, E., and MCHENLAND, J. *J. Am. M. Ass.* 1945, 131, 434.
8. SADDY, J. F. BLACK, F. O. and SETTSOCK, A. *Lab. J. Biol.* 1945, 68.
9. SCHWABER, H. B. *Surgery* 1945, 903.
10. T. LLOYD, GORDON. *Surg. Gyn. Obst.* 1945, 74, 375.
11. THEODOROFF, T. D. *Surgery*, 1945, 907.
12. WALTER, LLOYD E., and COLL, WALTER H. *Brit. J. Surg.* 1945, 1, 50.

# THE DISTRIBUTION OF NERVES IN THE ADULT HUMAN MYOMETRIUM

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ACCORDING to recent summaries (3, 12) no detailed descriptions of the anatomical relations of the intrinsic nerves to the muscle and vascular structures of the uterus have been published. The information compiled in these summaries is general and to some extent confused. A study of large nerve trunks and branches in the adult human endometrium was reported recently by State and Hirsch. They observed large nerve trunks and smaller branches in the basal portion of the endometrium and traced the terminal branches of the nerve fibers to blood vessels near the endometriomyometrial junction. Some fibers seemed to end freely in the stroma of the endometrium. Large nerve trunks in the myometrium, according to their observations, contained many nonmyelinated and some myelinated fibers. The nonmyelinated fibers, accordingly, agreed in structure with vasomotor nerves elsewhere in the body, are postganglionic, and probably belong to the sympathetic nervous system. The myelinated fibers had the anatomical structure of sensory nerves. According to Albert Kuntz, an abundance of nerve fibers has been observed in the uterine muscle and along the blood vessels. No one, however, has traced the course of these fibers in the myometrium for the purpose of establishing details of distribution and anatomical connections. These details have significance because physiologically, according to Kuntz, the sympathetic nerves supplying the uterus exert a motor influence, the parasympathetic nerves an inhibitory effect. Also, the sympathetic supply includes the vasoconstrictor, and the parasympathetic supply the vasodilator fibers for the female genitalia.

From the review by Daron and his study of the endometrium in *Macacus rhesus*, the fol-

lowing general statements of the arterial circulation in the uterus are obtained. Branches from each laterally placed uterine artery pass inward and upward and encircle the wall of the uterus. They penetrate the inner portions of the myometrium and continue into radial divisions that supply the coiled or spiral arteries which extend as true terminal vessels into the outer portions of the endometrium. Smaller arteries of a second type supply the basal zone of the endometrium. Daron stated that the flow of blood through the spiral arteries is controlled by (1) tortuosity, and (2) contraction of the radial arteries in the inner fourth of the myometrium. These constrictions, according to Daron, produce at the onset of menstruation an ischemic necrosis of the superficial part of the endometrial mucosa. The mechanism responsible for this constriction of the radial arteries is not clear, except on the general basis of hormonal action. Daron stated that the basal arteries are not involved in these cyclic changes.

Jones and Brewer reconstructed from serial sections a model of a radial artery and the endometrial distribution of its spiral artery branches in the human uterus. They also described a constriction of the spiral vessels in the myometrium near the endometrial edge. These authors and others believed that constriction of the spiral arteries is important in the functional activities of the uterus and is accomplished through some hormonal action. Brewer observed an association between rhythmic changes in the fragility of the capillaries of the skin and the menstrual cycle. He concluded that the increased ease with which capillary hemorrhages are produced in the skin just before and at the onset of menstruation is due probably to a vascular spasm. This association of systemic vascular activity with menstrual periods indicates a generalized instead of a localized (uterine) vascular phenomenon.

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Aided by the Winfield Peck Memorial Fund  
Dr. Martin, The John Jay Borland Fellow



Fig. 1

Fig. 1 Photomicrograph illustrating several segments of large nerve trunk extending diagonally through the inner portion of the myometrium, associated with group of radial and spiral arteries and entering the basal portion of the endometrium. A smaller nerve trunk is below on the right near another radial artery. (Enlargement of low power photomicrograph.) Insert in upper left corner. X7. Section from opposite angle. Insert corner of photomicrograph, containing nerve trunk in the myometrium and its trans-

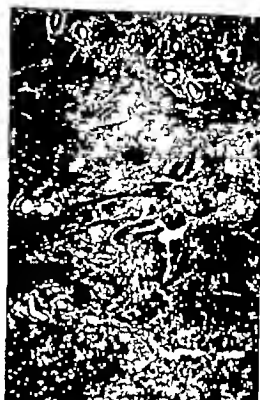


Fig. 2

verse sections of spiral (or radial) arteries associated with another nerve trunk. Below the latter nerve trunk and in the angle between the two arteries is sensory capsule.

Fig. 2 Photomicrograph illustrating small nerve trunk, passing through the myometrium and approaching radial artery. Nerve trunk like this traverses the deeper portions of the myometrium in similar manner. At the base of the endometrium is small nerve trunk. (Enlarged from low power photomicrograph.)

An investigation of neurovascular relations in the uterus, therefore has merit because of the known physiological vasomotor action of these nerves and its implications in uterine function and also if such anatomical relations are found the concepts of vasomotor control which are accepted for other tissues of the body may be applied in the understanding of uterine physiology.

#### MATERIAL AND METHODS

The distribution of the nerves in the adult myometrium was studied in sections cut serially and stained according to Goldner's modification of Masson's trichrome staining method

Mature nulliparous uteri were used, the one obtained postmortem from the body of a woman aged 19 years, the other removed surgically from a woman aged 36 years. They had no unusual changes. Each uterus was opened by crucial incisions of the anterior wall and was fixed in Bouin's solution at icebox temperature for 3 days. Then the uterus was cut longitudinally into four pieces and fixed for 3 more days.

Blocks measuring 1 by 0.8 by 0.8 centimeter for embedding were cut from the lateral anterolateral and posterolateral walls begin-

Modified aqueous solution of trioxycarbol, 10 c.c. solution of formaldehyde, 25 c.c. and glacial acetic acid.

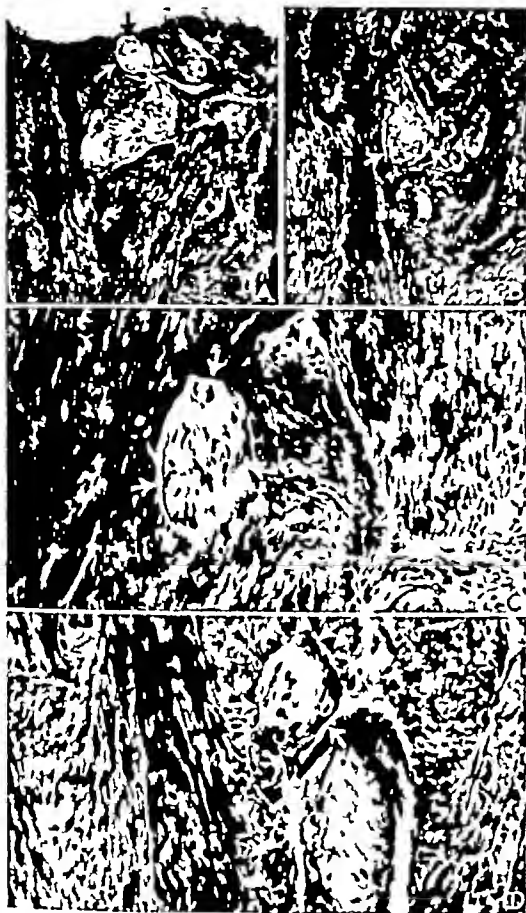


Fig 3

Fig 3 Photomicrographs illustrating nerve trunks in the myometrium of the uterus A,  $\times 85$ , a large nerve trunk associated with blood vessels, B,  $\times 85$  and C,  $\times 145$  nerve trunks in the muscle tissues, and D,  $\times 180$ , a small trunk near a blood vessel

Fig 4 Photomicrographs illustrating small nerve trunks



Fig 4

which in the inner fourth of the myometrium made serial contacts with radial or spiral arteries A,  $\times 187$ , two segments of a trunk near a venous channel, B,  $\times 155$ , two segments of a trunk in the muscle tissues, and C,  $\times 155$ , two segments of a trunk representing its approach to and egress from a radial artery

ning at the level of the internal os These blocks were fixed for an additional 48 hours in Bouin's solution, embedded in celloidin and paraffin according to the method of Bensley and Bensley and sectioned serially at 8 microns thickness With Goldner's modification of Masson's trichrome stain the axis cylinders of the nerve fibers are pale red, the neurilemma sheaths, pale green, the perineurium and endoneurium, purple-red, the fibrillar connective tissues, bright green, and the smooth muscle, brick-red

#### OBSERVATIONS

Large nerve trunks extend upward and inward in the lateral wall of the body of the uterus and divide into smaller trunks which penetrate the inner portions of the myometrium The large trunks lie in the periarterial fibrous tissues (Fig 3, a) for certain portions of their distribution, but at other levels (Fig 3, b, c, d) they pass directly through the muscle tissues of the myometrium The smaller trunks in the outer portions of the myometrium also extend through the muscle and



Fig. 4a



Fig. 4b



Fig. 4c

make contacts with arterial branches (Fig. 2). In this way single nerve trunks establish vascular connections with many arterial branches. This manner of distribution is noted especially in the inner fourth of the myometrium where the nerve trunks connect with several or a series of radial arteries (Fig. 4 c Fig. 5 a)

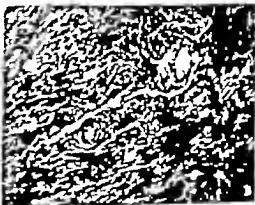
Fig. 5. Photomicrograph, X 87 illustrating nerve trunk relations with radial or spiral arteries. A, Two separate nerve trunks near one of these vessels; B, small nerve in the adventitia of an artery; C, small nerve near an artery and in the adventitia, sensory corpuscle.

Between the vascular contacts, the nerve trunks extend through the muscle with little associated stroma (Fig. 4 b) or are embedded in the fibrous connective tissues between muscle bundles and in tissue crevices about venous channels (Fig. 4 a). Small twigs (Fig. 5, b and c) are given off at various levels. Some large nerve trunks after connections with blood vessels (Fig. 1) pass through crevices at the endometriomyometrial junction and are distributed to the endometrium.

The nerve trunks in the inner fourth of the myometrium pass vertically for considerable extents. They make contacts with the radial arteries before these vessels divide into the



A



branchings of radial arteries into spiral arteries. At this level nerve trunks extend from one system of vessels to another in series. B. Photomicrograph, X 187 illustrating structure considered to be sensory corpuscle in crevice of the myometrium.

Fig. 6 A. Photograph of cleared segment from the inner fourth of the myometrium and endometrium of uterus whose uterine arteries had been injected with 5 per cent solution of rhodine dissolved in acetone and containing retamine blue. B. The photograph illustrates the

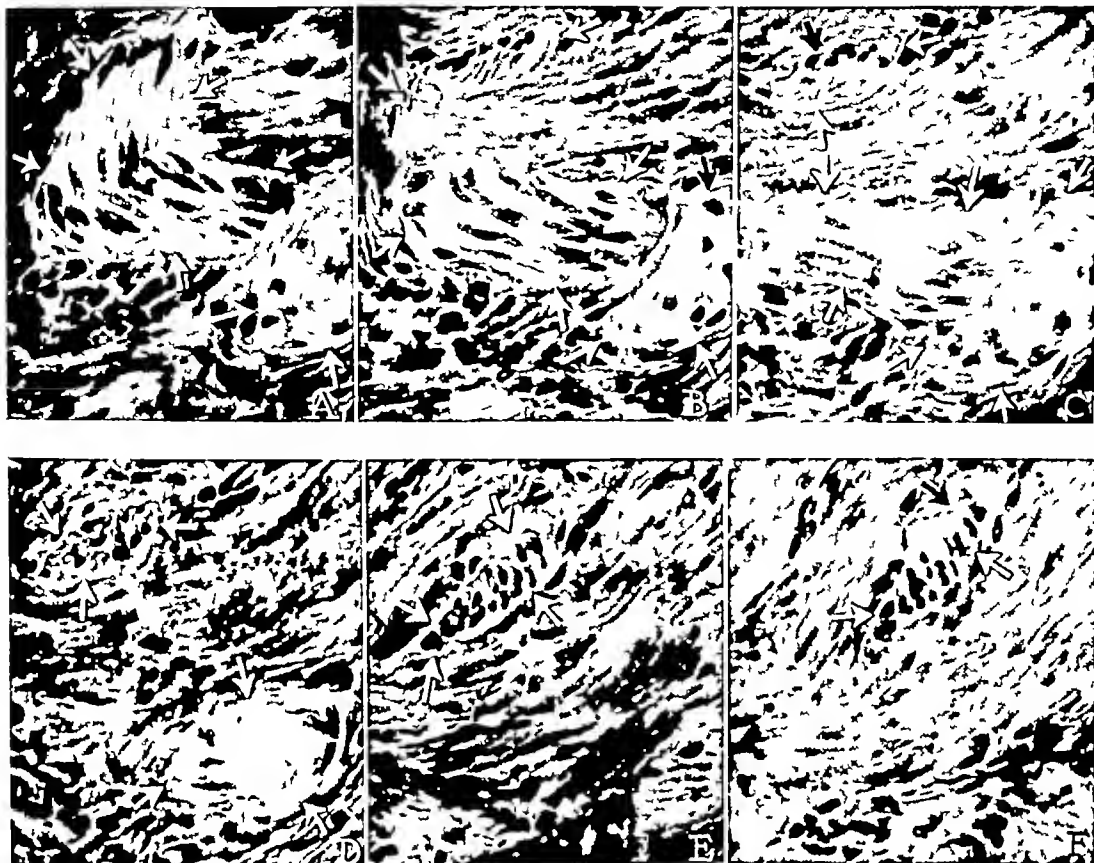


Fig 7 Photomicrographs,  $\times 340$ , illustrating a corpuscular sensory organ and its nerve trunk connection in consecutive serial sections. The series is unbroken to E. One section between E and F was not photographed, to avoid duplication, and one after F had only a small oval mass of

fibrillar tissue, at the tip of the corpuscle. At A, fibers are streaming up to the corpuscle from a nerve trunk, at B, only a few fibers remain, C and D, include the corpuscle and also the nerve trunk. E and F, illustrate the more distal portions of the corpuscle.

spiral branches to the endometrium and some also connect with the basal arteries. They follow the same general pattern of distribution, making contacts with a series of blood vessels and between the vessels passing through the myometrium. A single nerve trunk was traced through its contacts with five radial arteries. The association of nerve trunks with radial arteries was investigated also by tracing spiral arteries in serial sections from the endometrium into the myometrium. A nerve trunk or branch was demonstrated with many of these vessels. Those without may have had small nerves that escaped observation.

The search for nerve ganglia along the nerve trunks in the body of the uterus was futile. At

some levels the nuclear content of the nerve trunks appeared to be greater than at other levels, but no significance was attached to this variation in structure. Small nutrient arteries were present at various levels in large nerve trunks. The actual endings of the nerves in the walls of blood vessels and in the myometrium, except as mentioned later, were not demonstrated by the staining methods used in this study. Emphasis in the project was on the general distribution of the nerves and their anatomical relations to the blood vessels and muscle tissues of the uterus, for which the trichrome stain was adapted.

The presence of myelinated fibers in nerve trunks of the uterus has been recognized by

Dahl Mabuchi and others. These fibers have the anatomical structure of sensory nerves and like sensory nerves in other tissues of the body should have sensory nerve endings. Nerves to the large blood vessels of the extremities according to L. Hirsch contain both myelinated and nonmyelinated fibers. He found that the afferent fibers always were myelinated and that the endings in the walls were (1) branchings and coils of individual nerves without capsule and (2) typical lamellar corpuscles. The corpuscles varied in size and form and consisted of a peripheral layer of concentrically arranged spindle cells. In the center in addition to the nerve coils were plump darkly stained oval nuclei. These receptor organs resembled the Vater Pacinian corpuscles, the Krause nodes, and intermediary forms. Their maximum diameters ranged from 0.08 millimeter to more than 1 millimeter. Dahl did not find nerve endings in the uterus. Keiffer however described corpuscles of the Vater Pacinian varieties in the cervix and others in the myometrium.

In our study of the distribution of nerves in the myometrium small ovoid structures were found to extend a short distance from the margins of nerve trunks into the muscle tissues (Fig. 6 b) and into the adventitial coats of medium sized arteries (Fig. 5 c). One of them lying in a crevice in the muscle (Fig. 7) was traced directly to a nerve trunk. Others, after their tissue structure had been recognized were not so clearly identified with nerves. The encapsulated corpuscles found were about 80 to 90 microns long 30 to 35 microns wide and 15 to 18 microns thick. A cluster of small darkly stained, compact oval nuclei was in the center of the corpuscles and a small amount of fibrillar stroma was along the margins and at the tip.

#### SUMMARY AND CONCLUSIONS

Large nerve trunks enter the body of the uterus from below and laterally. They extend along the branches of the uterine artery then pass through the myometrium to join with other arterial branches, and divide into smaller

trunks that are distributed in a similar pattern. In the inner portion of the myometrium nerve trunks extend through the muscle and connect with a series of radial arteries. Many small branches whose ultimate endings were not determined are given off by the nerve trunks to blood vessels and muscle tissue. The presence of the small branches suggests an even more extensive vascular and muscle tissue distribution than actually was demonstrated by this study. Large nerve trunks also extend into the endometrium. The nerve trunks contain nonmyelinated or vagomotor and myelinated or sensory fibers. In the search for sensory end organs, corpuscles of the Vater Pacinian variety were found in crevices of the muscle tissues and more often in the adventitia of branches of the uterine artery. They were oval structures about 90 microns long 35 microns wide and 18 microns thick. The center had a cluster of compact oval nuclei and the periphery was a small amount of fibrillar stroma.

The abundance of nerves in the body of the uterus and the connections they make with branches of the uterine artery especially in the inner fourth of the myometrium where they connect with series of radial arteries, seems to provide a nervous tissue medium for effecting a control of the vascular phenomena which are associated with uterine physiology.

#### REFERENCES

- BRIDGES, R. R., and BRIDGES, S. H. A Handbook of Histological and Cytological Technique. P. 30. Chicago University of Chicago Press, 1934.
- BURDET, J. I. *Am. J. Obst.* 1935, 46: 977-8.
- FRANK, W. H. and HIRSCH, LOUIS F. *Am. J. Path.* 1941, 7: 721-739.
- DALL, W. *Zentralblatt Gyn.* 1916, 24: 539-60.
- DARBY, G. H. *Am. J. Anat.* 1915, 25: 349-9.
- GOULDEN, J. *Am. J. Path.* 1935, 41: 37-443.
- HIRSCH, L. *Arch. Klin. Chir.* 1926, 30: 5-39.
- JONES, H. O. and BEE, L. J. I. *Am. J. Obst.* 1932, 35: 839-850.
- KEIFFER, M. H. *Bull. Acad. Belgique.* 1934, 4: 47-50; 1936, 6: 305-320.
- KUWABE, MASATAKE. The Autonomic Nervous System. Pp. 308, 311. Philadelphia: Lea & Febiger, 1930.
- MARICIC, KOSUOKO. *Int. Med. Fak. Univ. Tokyo.* 1944, 3: 495-495.
- S. T. D. and HIRSCH, LOUIS F. *Arch. Path. Chir.* 1941, 12: 939-950.

# ANTERIOR SACRAL MENINGOCELE

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ANTERIOR sacral meningocele is a rare condition which is of importance only because of the symptoms it may produce and because if unsuspected, misdirected treatment may lead to meningitis. Review of the literature reveals a total of 23 cases, including ours. Eighteen of these were treated, with a mortality of 44 per cent. Eight were cured and 2 remained the same. A proper note of caution in the treatment of meningoceles was early sounded by Tulp when, in 1652, after an unhappy experience with a posterior meningocele, he said, "Beware, Oh surgeons, lest you open anything improperly which may easily kill a person."

In 1837, a distinguished surgeon, whose name at his own request was omitted (1), reported a case discovered at autopsy in a patient who had died 4 days following delivery in which was found a large cyst filling the hollow of the sacrum that prevented normal delivery. This case was mentioned in 1858 by Buhl (2), credit being given to Bryant who presided over the meeting of the London Medical Society before which the case was presented. In 1871, Emmet described a case in which he aspirated 3 inches beyond the anus a tumor which he took to be a kidney cyst and the patient died of "uremia." Autopsy revealed that half of the three lower sacral vertebrae were deficient on the right side, and the pedicle of a cyst that filled the pelvis passed through a funnel-shaped opening into the spinal canal in this area. He suggested that the septum between the 2d and 3d sacral foramina on the right had not formed, thus leaving a defect through which the sac herniated and that the larger defect was due to absorption of bone because of pressure by the sac. Coqui, describing Hofmohl's case (1878) stated that the tumor reached up to the iliac fossa, that "part of the sacral bone was lacking, and an intervertebrale foramen enlarged." The treatment was not discussed. Hugenberger, in 1879, described a case of a woman with pregnancy, delivery, and death from "peritonitis." The ruptured meningocele containing cauda equina was found at autopsy. Lohlein (1895) reported a case com-

plicating pregnancy in which he aspirated the tumor three times, opened it through the vagina, and later opened it through the rectum with subsequent healing. Cerebrospinal fluid was obtained on the first two punctures, pus thereafter. As the patient did not develop meningitis, closure of the pedicle must have occurred. Kroner-Marchand (1881) aspirated, then opened an anterior sacral meningocele through a vaginal incision with resultant meningitis and death. Thomas (1885) relates the history of a patient, a woman of 28 years, who presented a cyst filling the hollow of the sacrum lying posterior to the rectum. The lesion was untreated and its character can only be surmised. He reports in detail the case history of a girl of 19 who was found to have a cyst attached to the hollow of the sacrum that pushed the uterus and rectum forward and to a very great extent "occluded the vaginal canal." The cyst was first typed with production of fever for several days. Some months later she was operated upon through the vagina, the sac opened and within 24 hours its walls sutured to the vaginal mucosa. The patient died of infection and with symptoms suggestive of "tetanus," probably meningitis. The first report of treatment of the condition through a dorsal incision was in 1903 when Pupovac performed the operation, resecting part of the wall of the meningocele and closing the remainder by suturing it together, with resultant cure. In the same year Robinson, operating upon an 11 months old infant, ligated the pedicle of a similar tumor with silk. The child died with meningitis 10 days later and autopsy revealed a defect in the right side of the 12th thoracic and all of the lumbar vertebrae with protrusion of the sac in this area. The pedicles of the transverse processes of these vertebrae were absent and the vertebral bodies were irregular and fused. Willard's case (1904) was untreated and the subsequent course not known. Nieberding (1904) visualized the meningocele by laparotomy but did not touch it. After aspiration later, further treatment was refused. Neugebauer (1905) reported aspiration of such a tumor in a patient who refused radical treatment. He states that the patient died 3 weeks later by accident. Grossman (1906) successfully treated a patient by exposing the tumor through a posterior incision, cutting the pedicle and sewing

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Aided by The James and Elizabeth Inglis Fund for Surgical Research.





Fig. Anteroposterior view of the pelvis showing appearance of the sacrum.

It is the periosteum of the sacrum. In this 6 months old baby the tumor presented itself in the right gluteal region. Its pedicle passed through the greater sciatic foramen into a defect in the three lower sacral bodies on the right side. Coqui (1916) summarized the literature up to that time and reported a case of his own in which, at laparotomy, he cut the pedicle and tamponaded it with gauze. A fistula formed which drained spinal fluid for 6 months, then healed, and the patient had no further trouble. He emphasized caution in treating these tumors, feeling that they should be left alone if they caused no symptoms. He stated that it might be better to do a cesarean section and sterilization when pregnancy occurred, leaving the tumor alone. Roux (1908) described the case of an 8 year old boy who complained of constipation since birth, with frequency and incontinence of urine. After aspirating the tumor twice through the left hip region, he attempted injection with solution of iodine potassium iodide and glycerine. The child developed violent pain after cubic centimeters had been injected and although 160 cubic centimeters of fluid were aspirated, he had violent headaches for 3 days. Through a lower abdominal incision the neck of the tumor was then cut and sutured with catgut and good recovery was made. Weber (1911) reported the case of a woman 29 years old with double vaginas and double uterus with a cystic tumor filling the pelvis. This was removed by laparotomy. The pedicle of the tumor lying in the median

line at the inferior part of the sacrum was ligated. Meningitis supervened, but the patient recovered. Kennedy (1926) reported excision of a rectal polyp apparently arising from the coccyx in child of 22 months. Clear fluid flowed from the pedicle. The child died of meningitis and at autopsy the pedicle was found to be continuous with a meningocele which passed into a large opening in the anterior surface of the sacrum. Sabatini (1907) removed a posterior meningocele in a child of 3 months. Vomiting and distention developed. Rectal examination revealed a large retrovesical tumor with a pedicle leading to the sacrum, but because of the poor condition of the patient nothing was done and the child died 2 days later. At autopsy the anterior meningocele was found to contain neurofibros, cystic spaces lined with cylindric epithelium, and stratified squamous epithelium with all layers of the dermis, but no sebaceous or sudoriferous glands or cornification. He concluded that teratomatous formation existed. Denel (1928) also described a meningocele which presented over the sacrum with a pedicle that passed through the foramen suprapariforme. The pedicle was closed by suture ligature and plastic use of the surrounding soft parts. Postoperative x-ray film showed an anterior sacral cleft two fingerbreadths wide at the level of 1st sacral, becoming twice as wide toward the lower segments. Follow-up after 3 years showed no recurrence. He states that the operative treatment is justified only when conditions such as desire for pregnancy or complications resulting from displacement of surrounding organs are present. Drennan (1929) using the posterior approach opened a meningocele in a patient whose complaints had been increase in the length of the menstrual periods with passage of clots and pain and after removing the fold closed the wound loosely, not ligating the pedicle of the sac. Death resulted from meningitis. At autopsy the anterior part of the sacrum from the 3d sacral vertebra down was absent the sac protruding in this area. Posteriorly the laminae of the sacral vertebrae and the coccyx were present. Pick (1929) treated a 32 year old soldier who complained of lifelong constipation. After obstipation for 5 days and acute lumbar pain and headache he had temperature of 100 degrees, white blood cell count of 6400, and palpable retrorectal tumor by aspiration of the tumor through the rectum. Meningitis and death resulted, and at autopsy the coccyx and "some sacral vertebrae" were missing. The connection between the sac and the spinal canal was assumed but not demonstrated. Luth (1937), while doing an appendectomy in a 5 year old girl, palpated cyst

the size of a child's head in the pelvis. It was retroperitoneal and displaced the uterus and adnexa forward. When he attempted to enucleate it, it ruptured discharging a serous, clear fluid, and the cavity was found to connect with a wide fissure of the sacrum. Part of the wall of the cyst was resected and tamponage with iodoform gauze was carried out. Postoperative x-ray examination of the spine revealed absence of the spinous process of the last 2 thoracic vertebrae, asymmetry of the sacrum with a widely open hiatus sacralis. Death from meningitis occurred, and autopsy revealed an anterior sacral meningocele extending toward the right side of the pelvis. The author concluded that treatment of this condition should be conservative, and that, if symptoms made operation necessary, the posterior approach was best, with resection of part of the sacrum if necessary, as laparotomy constituted a greater risk on account of the large vessels. Santy (1938), using the posterior approach, dissected out the wall of an anterior meningocele, finding and removing two small dermoid cysts also. After operation the patient had headaches and temperature elevation to 104 degrees, with drainage of clear fluid from the wound. The temperature became normal in 1 month, but a fistula draining clear fluid persisted for 6 months. This patient's complaints before operation had been constipation and pain in the left hypochondrium radiating down the left leg. Examination had revealed a small swelling in the perineum and a retrorectal tumor. Neurological examination showed hypotonic but equal patellar reflexes and absence of the right Achilles reflex but no muscle weakness. X-ray examination showed loss of substance corresponding to the usual situation of the lower opening of the sacral canal, with deformity and deviation to the left of the last sacral vertebra. Microscopic section of the sac wall showed nerve cells and fibers, and areflexia and hyperesthesia of the lower extremities was noticed after operation, with gradual return of function.

Our patient, N. H. (488890), a 22 year old single, white, female student was first seen in June, 1941, complaining of constipation. She stated that she had been constipated "all her life," and in the last 2 years had required daily enemas. She had no bloody or tarry stools, no tenesmus or weight loss.

The past history was noncontributory except that the patient stated that she had always preferred to sit on one buttock or the other, having a vague sense of discomfort if she sat squarely. The family history was that one brother had died at the age of 22 months of "bowel obstruction," and a sister had died at the age of 10 months of spinal meningitis.

Physical examination was negative except for rectal examination, when a firm, slightly fluctuant, grapefruit-



Fig. 2 Barium enema showing compression of the rectum by the tumor.

size, nontender, slightly movable tumor was felt in the pelvis. No mass was palpable on abdominal examination. Neurological examination was negative. Review of the x-ray films showed profound deformity of the sacrum, suggesting nondevelopment of the right half, displacement of the left half toward the left, and displacement of the coccyx to the horizontal position. The rectum was displaced and compressed, and the sigmoid was displaced upward as was the small bowel. The left innominate bone was rotated somewhat and the sacroiliac joints slightly widened. The bone margins were smooth and not eroded. It was our opinion that the patient had a developmental lesion which might be a dermoid or an anterior sacral meningocele, and to gain perspective it was decided to follow her course for 2 months and repeat the barium enema and examination at that time to see if the tumor was growing.

The patient returned September 12, and the tumor showed no increase in size by physical examination. Because of continued constipation and the possibility of future interference with child bearing, she was advised to have the tumor removed.

At operation an incision was made through the lower right midrectus muscle thus exposing a retroperitoneal tumor, gray in color and fluctuant, which pushed the ureters and pelvic organs forward. It was clear that the tumor could not be adequately exposed by this anterior approach. Accordingly, the abdomen was closed and the patient turned on her face in the jackknife position. A vertical incision, just to the right of the midline over the coccyx was made and carried down to bone. The tip of the coccyx was removed, the tumor wall exposed, and clear fluid was



Fig. 3. Postoperative roentgenogram showing the position of the pedicle as marked by the silver clips.

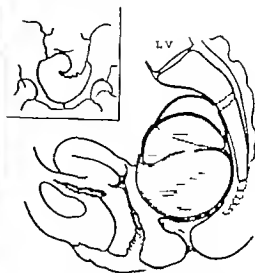


Fig. 4. Diagram to show configuration of the tumor. The dome of the tumor is at a higher level than shown here.

aspirated. When the meningocele was opened, 500 cubic centimeters of clear fluid was aspirated revealing a grapefruit size cavity which in turn opened its apex into a second smaller cavity which in turn opened into a third and smaller sac from which a pedicle passed into the spinal canal through an anterior sacral hiatus. No nerves were seen in the pedicle or sac. The pedicle was suture ligated with No. 1 black silk. On bilateral jugular compression, spinal fluid issued from the pedicle above the ligation. This opening was closed with two silver clips. A small metaphen-in-oil pack was then placed about the pedicle to create adhesions and the end of the pack was brought out through the wound. A portion of the sac was excised for microscopic examination and the wound was closed in layers with interrupted sutures of fine black silk. The patient was transferred to bed in the prone jackknife position, supported on pillows. The pathologist's report on the sac wall was: Dense fibrous connective tissue.

After operation the patient was kept in the prone jackknife position with her hips higher than her head for 3 days. She was then allowed to turn on her side occasionally, her hips being kept elevated, and after the 6th day was allowed to turn on her back to aid drainage from the wound and to allow the pelvic organs to fall back into place and obliterate the sac. The foot of the bed was lowered on the 13th day. Immediately after the operation the patient was started on a liquid diet without fruit juices, and was given paregoric 4

cubic centimeters four times a day to prevent bowel movements and contamination of the posterior wound. She had no bowel movements until paregoric was stopped and a general diet started on the 13th day and thereafter had regular bowel movements.

Her temperature rose to 100 degrees the first day, 101.6 the second day and thereafter ranged between 99 and 100.4 degrees until the 8th day when it fell to normal and remained normal. On the 3d day examination showed temperature of 100.6 degrees, white blood cells of 12,000. Although there were no signs of meningeal irritation, a lumbar puncture was done and spinal fluid, which was grossly clear, was allowed to drain through the needle until flow ceased 30 cubic centimeters being removed to relieve pressure on the ligated pedicle. Examination of the fluid showed 8 cells per cubic millimeter and culture showed no growth. Sulf. thiazole was started as prophylaxis against the development of meningitis, 3 grams being given initially and 1 gram every 4 hours thereafter until the 8th day when the dose was reduced to 4 grams per day. The white blood count on the 11th day was 9,600.

The anterior wound healed well. The posterior wound was kept walled off with oiled silk, the dressing being changed first on the 6th day. There was small amount of sanguinopurulent drainage about the pack at this time but the wound seemed to be healing well. The sutures were removed on the 8th day and on that day profuse watery

yellow drainage from the wound began. The pack was removed on the 10th day, and the drainage continued in gradually decreasing amounts. The patient was allowed up out of bed on the 14th day and went home on the 20th day. At this time there was a small amount of drainage from the wound daily. A 6 inch by 3 inch area of anesthesia on the posterior aspect of the left mid thigh extending around to the anterolateral aspect was noted on the 10th day and was present when the patient went home. The patient was seen at weekly intervals, and 3 weeks after she left the hospital the posterior wound was healed, the area of anesthesia was smaller, and there were no reflex or motor changes on neurological examination. She felt well and was ready to start back to school. Checkup examination on March 20, 1942 showed her to be in perfect general condition and the rectal examination disclosed only a vague sense of thickening behind the rectum.

#### OBSERVATIONS

Anterior sacral meningocele usually manifests itself within the first 3 decades of life. It occurs more frequently in females than in males, the ratio being 20:3 in the reported cases. The youngest patient was 3 months old, the oldest 36 years old. The meningocele enters the pelvis through an anterior sacral defect which is usually laterally placed and occurs more often on the right than the left side. However, the tumor may herniate through the sciatic foramen and present posteriorly. The presenting complaint is usually constipation, although in one case dysmenorrhea and increase in the length of the menstrual periods were noted. Diagnosis is suggested by a history of lifelong constipation, palpation of a fluctuant retrorectal tumor, and demonstration of deformity of the sacrum by the x-ray. The treatment should be conservative unless symptoms become severe or the danger of the meningocele complicating pregnancy arises. The operation consists in exposing the tumor, ligating and sectioning its pedicle. It is not necessary to excise the wall of the sac because it does not secrete spinal fluid. It seems better to approach the tumor through a posterior midline incision than through an ab-

dominal incision because it can be more easily visualized in this manner and there is less danger of damaging the great vessels, the pelvic organs, or the ureters.

#### SUMMARY

Anterior sacral meningocele is discussed, the literature reviewed, and a case with treatment described.

#### REFERENCES

- 1 "A Distinguished Surgeon," anonymous at his request, "as he was anxious the case should not be recognized by some parties to whom its publication might give pain." Case of deficiency of the anterior part of the sacrum, with a thecal sac in the pelvis, similar to the tumor of spina bifida. Reported to the Medical Society of London, November 27, 1837, Mr. Bryant presiding. *Lancet*, 1837, 1: 358-360.
- 2 BRYANT, T. Referred to by Buhl. Bericht ueber die Leistungen im Gebeite der Bildungsfehler und Foetalkrankheiten. Canstatt's Jahresh. Fortschr. ges. Med., 1858, 2: 24. Same case as in reference 1.
- 3 COQUI. *Zschr. Geburtsh. Gyn.*, 1916, 78: 609-631.
- 4 DEMEL, RUDOLPH. *Deut. Zschr. Chir.*, 1928, 209: 90-97.
- 5 DRENNAN, A. M. *J. Path. Bact., Lond.*, 1929, 32: 843-844.
- 6 EMMET, T. A. *Am. J. Obst., N. Y.*, 1871, 3: 623-631.
- 7 GROSSMAN, EMIL. *Jahrb. Kinderh.*, 1906, 63: 224-234.
- 8 HOFMOLL. *Medizinische Jahrbücher*, 1878, pp. 443-466.
- 9 HUGENBERGER, THEODOR. *Arch. Gyn.*, 1879, 14: 1-33.
- 10 KENNEDY, R. L. *J. Surg. Gyn. Obst.*, 1926, 43: 803-804.
- 11 KRONER, TRANGOTT, and MARCHAND, F. *Arch. Gyn.*, 1881, 17: 444-474.
- 12 LOHLEIN, H. *Gynäkologische Tagesfragen*, 4: 32-46. Wiesvanden J. F. Bergman, 1895.
- 13 LUTH, GEORG. *Zbl. Chir.*, 1937, 64: 15-19.
- 14 NEUGEBAUER, FRANZ VON. *Beitr. Geburtsh. Gyn.*, 1905, 9: 198-252.
- 15 NIEBERDING, WILHELM. *Münch. med. Wschr.*, 1904, 51: 1384-1386.
- 16 PICK, B. P. *Brit. M. J.*, 1929, 2: 46.
- 17 PUPOVAC, D. *Arb. Geb. klin. Chir.*, 1903, 1: 533-549.
- 18 ROBINSON, H. B. *Med. Press & Circ., Lond.*, 1903, 75: 477-478.
- 19 ROUX, SUZANNE. *Rev. méd. Suisse rom.*, 1918, 38: 47-71.
- 20 SABATINI, LUIGI. *Polinclinico*, 1927, 34: 254-265.
- 21 SANTS, P. *Lyon chir.*, 1938, 35: 446-448.
- 22 THOMAS, T. G. *Gaillard's M. J., N. Y.*, 1885, 40: 237-242.
- 23 TULP, NICOLAES. *Observations medicae Amsterd. Elzevir*, 1652.
- 24 WEBER, E. *Rev. fr. gyn. obst.*, 1921, 16: 377-392.
- 25 WILLARD, DE FOREST. *Ann. Surg.*, 1904, 39: 612-615.



Fig. 1.



Fig. 2.



Fig. 3.

Fig. 1. a, Case J. G. Preoperative ray film of right humeral stump at age of 7 years, April, 1931. b, Preoperative ray film at 13 years, March, 1934. c, 3 years after at reamputation. Preoperative ray film at 16 years, September, 1937. d, 3 years after at reamputation. e, Preoperative photograph showing bone protrusion, September 1937.

Fig. 2. a, Case J. L. P. Congenital amputation showing bone protrusion. Operative subperiosteal removal of bone. b, Protrusion due to bone overgrowth. The bone covered with granulations.

Fig. 3. Case 9, J. S. Bone protrusion. Note clamping cephalon.

# AMPUTATIONS IN CHILDREN

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**A**LTHOUGH amputations in children are not nearly so common as in adults, congenital deformities, osteomyelitis, and trauma often make them necessary. They are worthy of special attention because *amputations in children are different*. Apparently it has not been generally recognized that there is continued bone growth without equivalent soft part elongation which frequently causes unwieldy stumps, pain, and bone protrusion. These are so common that one should be impressed by the frequent necessity for reamputation.

The upper humeral, tibial, and fibular epiphyses are all centers of rapid growth, and each supplies more than 50 per cent of the growth of its bone. As the epiphysis is usually some distance proximal to the stump end, the blood supply remains intact following amputation, and therefore bone growth is not interfered with. On the other hand the lowered skin temperature and shrinkage around the end of the stump are evidence of muscle atrophy and diminished blood supply which probably reduces the soft part potential for growth. This may be the reason for the failure of soft part growth to equal bone growth. Commonly the bone is seen protruding from the soft parts but is still covered with tightly stretched skin. The next stage in the process is ulceration over the protruding bone. Eventually the bone perforates the skin, in which case soft granulations usually cover the bone.

In a series of tibial amputations seen by the author, 16 of 20 children had bone protrusion or painful long stumps with tightly stretched skin and soft parts (Table I). The cases observed include not only operative but also congenital amputations. Eight patients whose epiphyses were fused have had no difficulty with their stumps. In another series of cases it was found that only 5 of 20 femoral amputations had bone protrusion. This may be due to the very adequate thigh circulation and the relatively small amount of growth at the upper femoral epiphysis. Epiphysiodesis is therefore recommended as an adjunct to amputation in children in cases in which the section is through the tibia or humerus. This simple orthopedic procedure will prevent deformity by stopping further bone growth.

As can be seen in Table I, all patients, but Cases 1 and 20, were old enough so that an

"ideal" stump length could be obtained at the time of original amputation. This is usually possible after the age of 6 years. Optimum tibial length varies between 4 and 7 inches. If this length can be obtained, further growth is certainly not desired as it will make the use of a prosthesis difficult and painful. Therefore, epiphysiodesis, in addition to preventing bone protrusion, maintains the "ideal" tibial length. It should have been performed on these 2 patients (Cases 1 and 20) at the time of first reamputation. We presuppose that the remaining epiphysis of the severed bone is still open. This should be determined by x-ray examination, as the upper tibial epiphysis, for example, not infrequently remains open until the patient reaches the age of 24 years.

Fusion of the upper tibial or fibular epiphysis is a very simple procedure adequately described elsewhere (2, 3). In primary amputations it is usually better to wait about 3 weeks before epiphysial fusion is performed. But reamputation and epiphysiodesis may easily be done in one stage.

The approach to the upper humeral epiphysis is not described in the usual texts. The author has used short anterior and posterior paradeltoid incisions. A large amount of cartilage should be removed with a curette and the arm kept in a swathe for 3 weeks.

There is also an economic factor involved in these cases. Stump growth usually requires rapid change of prosthesis in the case of children, whereas the changes which occur are much less frequent when the growth is entirely above the knee joint.

Occasionally amputation will be done in children so young that an "ideal" stump length cannot be obtained. In these patients epiphysial fusion may be delayed until the optimum length has been reached and in the hope that reamputation will not become necessary. The epiphysis should be fused, however, as soon as the optimum length has been reached.

## SUMMARY

A résumé has been presented of 23 cases of amputation in children in which bone protrusion necessitated reamputation. The protrusion apparently was due to continued growth of an

TABLE I.—RESUME OF 23 CASES OF REAMPUTATION

Case	Sex	Site	Primary amputation		Reamputation		Comments
			Age	Reason	Age	Reason	
10	Male	R. humerus		Severe burn	20	Bone protrusion in stump	At each reamputation the stump is covered with the same flap
11	Male	R. humerus		Gas gangrene	16	Bone protrusion	Slut ulcer
12	Male	L. tibia		Trauma		Bone protrusion	2 pschymosis
13	Male	L. tibia	20	Unknown	26	Bone protrusion	Stump too long
14	Male	R. humerus		Gunshot	5	Pain	Very tight skin
15	Male	L. tibia		Trauma	11	Bone protrusion Tight skin	Pain and ulcer
16	Female	R. tibia		Congenital		Bone protrusion	1 shock removed
17	Male	R. humerus		Cutaneous	12	Bone protrusion	Pain granulations
18	Male	L. tibia		Trauma	26	Bone protrusion	
19	CR	Male	R. tibia	Congenital deformity		Growth	Stump too long epiphyseal
20	Male	R. tibia		Trauma	20	Growth	Stump too long
21	Male	R. tibia		Trauma	12	Bone protrusion	Pain, epiphyseal
22	Male	L. humerus		Trauma		Bone protrusion	Ulceration
23	Male	R. tibia	12	Trauma	20	Pain	Slut, pressure
24	Male	R. humerus		Congenital deformity		Pain, growth	Slut pressure, stump too long
25	Male	R. tibia	14	Trauma	16	Pain, growth	Stump too long
26	Male	L. tibia		Unknown	8	Pain	Tight skin
27	Male	L. tibia		Trauma	12	Ulceration	Pain, stump too long
28	Male	R. tibia	20	Unknown		Pain	Tight skin
29	Male	R. tibia		Congenital malformation		Bone protrusion	Pain
30	Male	L. tibia		Congenital deformity		Pain	Tight skin
31	Male	R. humerus		Trauma	10	Pain	Tight skin
32	Male	R. tibia		Unknown	16	Growth	Stump too long

\*Cases reported through kindness of Dr. Paul C. Calverton of Oklahoma Crippled Children Hospital and of Dr. Francis Carr of Hospital for Crippled and Crippled of New York.

open epiphysis without compensatory soft part elongation.

After the age of 6 years an ideal stump length can usually be obtained. Further growth is not desired.

Therefore, epiphyseal fusion has been recommended following amputation in childhood to pre-

vent deformity pain, bone protrusion, continued growth and reamputation.

## REFERENCES

- KENTZ, A. D., H. AND, R. C. *Ann. J. Surg.* 9:50-51 1713  
 FINKELSTEIN, D. B. *J. Bone Surg.* 9:53 5  
 J. ORT, S. A., F. H. *J. Bone Surg.* 9:50 447

# PRIMARY CARCINOMA OF THE APPENDIX RESEMBLING CARCINOMA OF THE COLON

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MUCH has been written concerning epithelial neoplasms of the appendix (1, 3, 6, 10, 11, 12, 13), but there is still considerable confusion with regard to the classification of these tumors. A simple yet workable classification would divide carcinomas of the appendix into 3 types: first, carcinomas of the carcinoid type (5, 7, 8), second, carcinomas of the cystic type producing pseudomyxoma peritonei (2, 4, 9, 14, 15), and third, carcinomas which resemble, both grossly and microscopically, those found in the colon and which will be referred to as the colonic type.

Our interest in the subject of carcinomas of the appendix of the colonic type was aroused by a recent case which emphasizes the importance of recognizing a carcinoma of this type.

## REPORT OF CASES

**CASE 1** The patient, a woman aged 69 years, had a 6 weeks' history of pain in the right lower quadrant with an occasional tarry stool. Two weeks previous to admission a mass was felt in the region of the cecum which was slightly tender yet movable. On examination a tender mass 3 by 4 centimeters in diameter was felt in the right lower quadrant of the abdomen. The leucocyte count was 11,200 in each cubic millimeter of blood. On roentgenological examination of the colon, the tip of the cecum was deformed by pressure apparently from what seemed to be an extrinsic mass. At operation the appendix was found to be very large. Examination of the appendix disclosed a polypoid mass which involved the proximal 4 centimeters of the mucosa (Fig. 1). Histological examination by the fresh frozen section technique disclosed an adenocarcinoma, grade 1—Broders' method—(Fig. 2), which had not yet begun to invade the musculature. This carcinoma was forming considerable mucus and was comparable both grossly and microscopically to those seen in the colon. In addition there was an inflammatory perforation of the tip of the appendix with periappendicitis. Because of the wide distribution of the carcinoma on the mucosa at the base of the appendix, the portion of the cecum surrounding the opening of the appendix was excised. No carcinoma was found in this specimen. The opening in the cecum was closed. The patient had an uneventful convalescence except for a slightly tender mass which could be felt through the abdominal wall lateral to the anterior iliac spine. On the 12th postoperative day this subsided under treatment with diathermy. The patient was dismissed from the hospital on the 21st postoperative day with the wound healed by primary union. Nine months later she was living and well.

A search of our files supplemented by further microscopic examination of suspected specimens disclosed that in the period from 1910 to 1941, inclusive, a diagnosis of carcinoma of the appendix had been made on 144 specimens removed at operation. Of this number 127 (88.2 per cent) of the carcinomas were of the carcinoid type, 12 (8.3 per cent) of the cystic, and 5 (3.5 per cent) of the colonic type. Only 5 specimens of primary adenocarcinoma of the appendix of the colonic type had been removed at operation. This includes the case which has been cited. A brief summary of the additional 4 cases follows.

**CASE 2** The patient, a woman aged 36 years, 6 months before had had two attacks of abdominal pain in the right lower quadrant with vomiting and fever. Each attack required morphine. During this period blood was passed in the stools. On examination there was found generalized abdominal tenderness. A roentgenogram of the colon showed an incompetent ileocecal valve with dilatation of the cecum. At operation a leiomyoma of the uterus was removed together with the appendix.

On gross examination, the distal 1 centimeter of the appendix was obliterated. Proximal to this obliteration in the middle third of the appendix was a tumor 1.3 by 0.5 by 0.5 centimeter. This disclosed histologically an adenocarcinoma, grade 1, which had involved the mucosa, submucosa, and musculature and also was forming good acini and much mucus.

The postoperative course was uneventful. Ten years later the patient was alive and well and abdominal hysterectomy did not disclose any evidence of the presence of carcinoma.

**CASE 3** The patient was a man, aged 60 years. Two months prior to admission, he had had generalized abdominal pain. One week after admission, he had pain in the right lower quadrant of the abdomen with elevation of temperature. There was no blood in the stools. A roentgenogram of the colon showed a deformity in the medial aspect of the cecum displacing the ileum toward the midline, suggesting a pericecal granuloma. The leucocyte count was 10,800 in each cubic millimeter of blood. At operation a tumor was found at the base of the appendix and cecum with much secondary inflammation. Ileocolostomy was done and 3 weeks later resection of the right portion of the colon was performed. The gross specimen consisted of 7 centimeters of ileum, 8 centimeters of cecum and the appendix. An adenocarcinoma, grade 1, was found at the base of the appendix extending into the cecum (4 by 3 cm). The lymph nodes were not involved. The patient had an uneventful convalescence. Three and a half years later, the patient was living and well.

**CASE 4** The patient, a woman aged 50 years, had pain in the upper part of the abdomen for several months requiring morphine 2 or 3 times a week. On examination,





Fig. 1.

Fig. 1. Papillary adenocarcinoma, grade of the appendix of the colonic type. This gross specimen as removed in Case.



Fig. 2.

Fig. 2. Section of papillary adenocarcinoma of the appendix. Well formed acini in which papillary projections are evident (Case ). Hematoxylin and eosin stain X45.

there as found tenderness, particularly on the right side. A normal leucocyte count as obtained. A roentgenogram revealed poorly functioning gall bladder with stones. At operation cholecystectomy and appendectomy were done. There were no other demonstrable lesions in the abdomen. The gall bladder disclosed the presence of chronic cholecystitis with stones.

On gross examination of the appendix, the lesion as found to be dilated, and at its tip was polypoid tumor 1.

centimeters in diameter. This revealed mucous-producing adenocarcinoma, high as graded because of the differentiation into well formed glands. The postoperative convalescence was uneventful. Four years later the patient was alive and well.

Case 5. The patient as seen, aged 46 years. He had had epigastric distress (periodic for 10 years) relieved by soda. Examination revealed epigastric tenderness. A roentgenogram of the stomach and duodenum disclosed duodenal ulcer. The leucocyte count was 10,000 in each cubic millimeter of blood on admission. At operation, duodenal ulcer was found, and partial gastrectomy as performed. Routine appendectomy was done. Examination of the stomach and duodenum revealed mild gastritis and duodenitis. Within the lumen of the appendix there as 5 millimeter projection, which revealed an adenomatous polyp showing early adenocarcinoma, grade (Figs. 1 and 2). The patient had an uneventful convalescence and as discharged from the hospital on the 10th postoperative day. A year later he as in good health.

TABLE 1.—COMPARISON OF THE THREE TYPES OF CARCINOMA OF THE APPENDIX.

	Carcinoid type	Cystic type	Colonic type
Location	Usually tip	Tip or base	Tip or base, more frequently base
Incidence	50 per cent	5 per cent	per cent
Gross character	Yellowish solid	Cystic, frequently on base of mucosa	Grayish, polypoid or ulcerating
Microscopic structure	Poorly formed acini, mucous secret over tumor. Radiation of gland cells, usually few chronic cells	Papillary projections fragmenting to cyst. Comparable to cylindrical carcinoma of ovary. Epithelial cells low because of destruction by mucus	Frequently well formed acini, mucous secret, lesions ulcerated. Comparable to carcinoma of colon
Malignancy	Few	Few	Variable
Mucus	None	Secretion large quantities	Secretion variable quantities
Metastases	T regional nodes in less than per cent	No called paraneoplastic metastases	T lymph nodes and liver

There are several inherent features about this type of neoplasm in the appendix which are outstanding and worthy of note. On gross examination the lesions may be either polypoid or ulcerative just as are carcinomas of the large bowel. Because of their frequent location in the base of the appendix, obstruction to the appendiceal lumen usually results early in the course of the disease. As a consequence, acute appendicitis—usually with perforation—is a common occurrence. This results in early operative intervention with removal of the diseased appendix including the carcinoma. It follows naturally that the prognosis is better than it is in carcinoma of the colon.

because the lesions are smaller when they are removed

Histologically, this carcinoma may be differentiated, producing well formed glands. On the other hand, the carcinoma may be quite undifferentiated and produce signet-ring cells. Usually variable amounts of mucus are produced by the neoplastic cells. Extra care is needed in the excision of this type of carcinoma of the appendix because such a neoplasm frequently involves the base of the appendix, occasionally extending into the cecum. If this is so, a more extensive resection may be necessary which would include a portion of the cecum.

Some, at least, of the colonic type of carcinoma originate on the basis of adenomatous polyps, as suggested by Case 5 in which there was carcinomatous change in an adenomatous polyp. The histogenesis appears to be comparable to that of a carcinoma of the colon. It is a well recognized fact that several carcinomas are likely to appear in the colon at the same or different times. For this reason greater care should be taken in the following up of this type of carcinoma of the appendix with special reference to the possible development of a carcinoma in some part of the colon or rectum.

The symptomatology which is found in this type of lesion appears to be twofold. Symptoms



Fig 3 Interior of the appendix showing an adenomatous polyp

of the first group are referable to obstruction of the appendiceal lumen with or without acute inflammatory changes in the appendiceal wall distal to the lesion. These symptoms may be exaggerated by perforation of the appendix. Symptoms of the second group are caused by the ulceration of the lesion with bleeding. The result is manifest by tarry stools.

A comparison of some of the more important points of differentiation between the three types of carcinoma of the appendix is set forth in Table I. Figures 5 and 6 represent the characteristic microscopic findings present in the carcinoid and cystic types.



Fig 4



Fig 5



Fig 6

Fig 4 Section of an adenomatous polyp in the appendix. Regions of malignancy are characterized by larger deeper staining nuclei as contrasted with the benign regions which show paler smaller nuclei. This lesion is in every way comparable to a carcinomatous polyp in the colon. Hematoxylin and eosin stain,  $\times 55$ .

Fig 5 Adenocarcinoma of the appendix grade 1 of the carcinoid type. The groups of small cells with deeply stain-

ing nuclei are apparent with very little evidence of formation of glands. Hematoxylin and eosin stain,  $\times 57$ .

Fig 6 Intracystic papillary adenocarcinoma grade 1. The papillary projections and the beginning infiltration into the wall of the appendix are to be seen. This type of neoplasm when it spreads to the peritoneum produces pseudomyxoma peritonei. Hematoxylin and eosin stain,  $\times 85$ .

## SUMMARY AND CONCLUSIONS

Primary carcinomas of the appendix may be divided into three types (1) carcinoid type (2) cystic type producing pseudomyxoma peritonei, and (3) colonic type. Five cases of the colonic type of carcinoma of the appendix have been presented and described. A table has been compiled to present the characteristic features in each of the 3 types of carcinoma of the appendix.

## REFERENCES

- BRUNER, I. *Berl. Klin. Wochs.* 33, 9 6 6-6 2.  
 CHAFFIN, J. S., and LEGRAND, R. H. *Arch. Surg.* 91, 45 55-73.

3. ELLIS, A. W. *Ann. Surg.* 90, 27 545-574.  
 4. HALL, D. P. *South. Surgeon*, 94 107 291-292.  
 5. HALL, A. *Texas. Virchow's Arch.* 3 241 85.  
 6. HERRN, J. *Ed. Char.* 93, 6 2601-2603.  
 7. HORTON, R. A., DOUGLASS, M. B. and M. W. J. C. *Arch. Surg.* 91, 45 6 3-6.  
 8. LAMORE, E. O. *Am. J. Surg.* 94 51 424 429.  
 9. MASON, J. C., and HARRICK, R. A. *Surg. G.* (Obs.) 93, 90 3-2029.  
 SCHILLER, F. C. *Minnesota M.* 940 3 70 725.  
 SKILVORN, J. *Ann. Surg.* 91, 40 274-274.  
 1. VANCE, C. A. *Am. J. Surg.* 93, 44 851-861.  
 3. WALLLEY, C. P. O. *Practitioner Lond.* 95, 1 731-739.  
 4. WARD, T. R. and FRIDLEY, D. W. *Am. J. Surg.* 1917 27 5 8-5 5.  
 5. WOODRUFF, R., and M. DONALD, J. R. *Surg. G.* (Obs.), 91, 7 730-733.

# INFILTRATION THERAPY OF ACUTE TENDINITIS WITH CALCIFICATION

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THE first descriptions of acute tendinitis with calcification were concerned with its occurrence at the shoulder joint. It was not until later, with the development of roentgenology, that it became possible to diagnose its existence in other locations, where its similarity linked it with the condition found in the shoulder.

A review of the literature on this subject indicates that the earlier investigators were not in a position to make a precise differential diagnosis of the multiple periarticular lesions of the shoulder joint. Therefore, their interpretations were often erroneous and their diagnoses inaccurate.

In the beginning of the nineteenth century Cowper, and later others, attributed most of the posttraumatic lesions of the shoulder to dislocation of the tendon of the long head of the biceps. Jarjavay, in 1867, denied the existence of dislocation of the biceps tendon and concluded that bursitis was misdiagnosed as a tendinous dislocation. On the basis of a few clinical cases and also anatomical dissections, he gave a rather precise description of bursitis at the shoulder. One of his patients had serous effusion in the bursa and was treated by repeated evacuation of the fluid by means of "puncture with a bisturi."

In 1872 there appeared the classical work of Duplay, who described a new clinical entity, which he called "périarthrite scapulo-humérale," later named after him, "morbus Duplay." Most of Duplay's cases were posttraumatic, and it is evident that his "périarthrite scapulo-humérale" included fractures, tendinous tears, tendinitis with calcification, bursitis, periarticular changes, which we now classify as "frozen shoulder," and probably also many other diseases of the shoulder.

Before Duplay, a great number of shoulder lesions were considered due to "rheumatism." In his first cases Duplay suspected intra-articular fibrous ankylosis because of the cracking sound produced during manipulation under chloroform. A postmortem examination performed in 1870 on one of his patients, whose shoulder had been manipulated under anesthesia because it was stiff

following a reduced dislocation, proved to him that the changes were periarticular, and not a true intra-articular ankylosis. Of especial interest is the following conclusion of Duplay: "In fact, one can admit that there exists besides the scapulohumeral joint itself a second articulation between the inferior surface of the acromioclavoid vault and the upper end of the humerus, which is covered by its periosteum and by the tendons inserting themselves over the tuberosities. All the motions of the scapulohumeral joint are associated with corresponding mobility in this second articulation which is located externally to the first, in other words, the upper end of the humerus glides beneath the acromioclavicular vault."

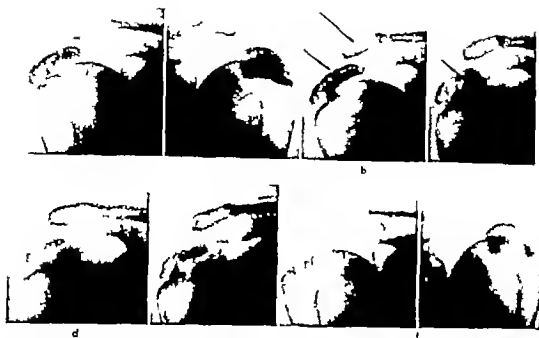
Fifty-six years later, Codman (1934) likewise considered the subacromial bursa "in fact a secondary scapulohumeral joint."

Duplay's treatment consisted of manipulation under chloroform followed by exercises. In 1878 Desplaces described his experiences with "morbus Duplay." He emphasized that periarthritis is not exclusively a local lesion of the bursa, but rather a manifestation of generalized *dialhèse rhumatique*. He reported 2 cases in which he stressed the simultaneous arthritic involvement of the other joints, muscular atrophy, tender brachial plexus, and other trophic changes. One of his patients apparently also had severe herpes zoster over the shoulder and the back. The treatment of Desplaces, however, was the same as that of Duplay, and likewise consisted of repeated manipulations under chloroform.

Putnam, in 1882, introduced "morbus Duplay" into Boston. He did not quite agree with Duplay's view that manipulation is the only rational therapy, since one of his patients recovered after being "left entirely to himself." Nevertheless, most of his patients were subjected to manipulation under ether. This procedure became the routine treatment in Boston, until the early days of Codman.

With the advent of roentgenology it became possible to observe periarticular shadows at the shoulder joint, which were thought to be fractures. During the first years of the twentieth century the designation "périarthrite scapulo-humérale" no longer satisfied the clinician. At-

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Fig. 2. Case 2, L. L. a, Roentgenogram of both shoulders taken on May 19, showing large dense calcareous deposit in both shoulders. b, Shows that the point of the first needle as incorrectly introduced (upper needle) striking the acromion. The second needle as properly inserted, penetrating toward the center of the calcareous deposit, but its point did not quite reach it. c, X-ray picture immediately after aspiration of 0.5 cubic centimeter of calcareous material. Note that the point of the needle now rests in the center of the deposit, and the large calcareous material is still demonstrable in spite of aspiration and infiltration treatment. However it appears to be more dense

and spread over somewhat larger area, as compared with the film, a, prior to aspiration and infiltration therapy. d, X-ray picture 3 days after the infiltration therapy. Note the fragmentation of the calcareous deposit, which appears to be more dense and spread over wider area. e, X-ray picture 3 weeks after the infiltration therapy shows further spreading and fragmentation of the calcareous deposit. f, X-ray pictures of both shoulders, 1 month and 3 days after the operation. Note practically complete disappearance of the deposit on the right treated side and no change over the left shoulder, both treated only with physical therapy.

tempts were made to discard morbus Duplay and to consider what was once diagnosed "peri arthritis scapulohumeralis," a periarthritic fracture which Duplay and his contemporaries were unable to diagnose.

Pourtin in his doctorate thesis (1901) entitled "About the Unknown Partial Fractures of the Upper End of the Humerus in the So-Called Primary or Secondary Periarthritis of the Shoulder" recorded 3 cases with fracture of the greater tuberosity, all of which were diagnosed as "morbus Duplay" before roentgenograms were taken. Pourtin expressed considerable doubt about the existence of bursitis, whether as primary lesion or of posttraumatic origin and thought that all these cases represented fractures. Obviously his teachers, Testut and Jacob, must have shared his opinion. The tendency to recognize fractures was so prevalent at this time that probably the calcareous deposit was also mistaken for a fracture.

In 1904 Codman called the term periarthritis a sort of surgical wastebasket in which throw our diagnostic failures. Two years later he described the anatomy of the subdeltoid bursa and opined that subdeltoid bursitis is far more common than any other lesion of the shoulder. Strangely enough there was no mention of the calcareous deposit in this article although reference was made to the fact that frequently there was evidence that a chip of bone was torn from the tip of the tuberosity at the point of insertion of the supraspinatus.

Several cases in which open operation had been performed were included in his paper. One (operated upon by Dr. F. B. Harrington) yielded "staphylococcus bearing pus." In a chronic case straw-colored fluid was present. Two patients were found to have a split in the capsule between

\*Codman must have been aware of the existence of the deposit, since he was present at the operation upon Patient 1, killed in May, 1905.



Fig 2 Case 3, H I. a, Roentgenogram of right shoulder with needle in center of the deposit before infiltration therapy. Note the presence of a deposit also over the left shoulder, a right, which was completely symptom free at that time. b, Roentgenogram of right shoulder 5 days after infiltration therapy. Note fragmentation and spreading of the deposit over a much larger area and beginning of absorption. c, Roentgenogram of right shoulder 4 months after infiltration therapy. Note practically complete disappearance of the deposit. d, Roentgenogram of right shoulder, 1 1/2 years after infiltration therapy. Note complete disappearance of the deposit on the right side. X-ray picture of the left shoulder taken at the same time showed the same findings as in a, at right.

the tendons of the supraspinatus and infraspinatus." This tendon rupture was also noted in 5 cadavers. Intra-articular fibrous bands and adhesions were often observed both at operations and also in anatomical material. Careful dissection on one cadaver showed "that the subdeltoid adhesions alone maintained the limitation of abduction and external rotation."

Painter (1907) seems to have been the first to report operative findings in a case of acute peri-articular calcification at the shoulder diagnosed roentgenologically before the operation. The pa-

tient, a physician, 37 years old was operated upon in the presence of Codman on May 17, 1905. The calcareous material was removed, and the patient sustained prompt relief. The operative findings were also given in 3 other similar cases. The deposit consisted mainly of calcium phosphate, also calcium carbonate, and traces of magnesium.

In 1908 there appeared another very extensive paper by Codman, based on observations of 75 painful shoulders. The term "subacromial" was offered as a substitute for "subdeltoid," and it was

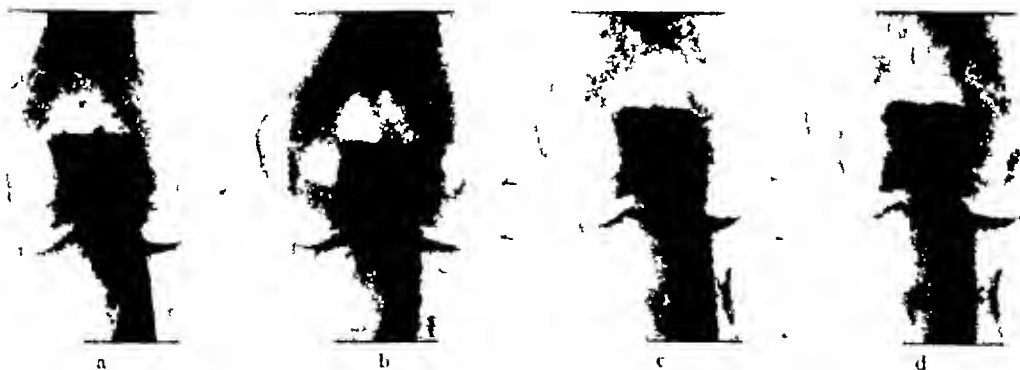


Fig 3 Case 17, K M. a, Roentgenogram of left elbow showing a small calcareous deposit (arrow) near lateral epicondyle. Note that the shadow is rather small and well outlined. b, Roentgenogram of same elbow 3 months later during very acute stage, showing considerable increase in the

size of the deposit which also became more diffuse. c, Same elbow 10 weeks after infiltration therapy shows only faint traces (arrow) of the deposit which hardly not capable of spread over a wide area. d, Same elbow 1 month after infiltration therapy shows complete disappearance of deposit.



Fig. 4. Case 3, G. C. a, left, Roentgenogram of the trochanter of the left femur during acute stage, showing large bony calcareous deposit (arrow). b, X-ray picture 5 days after infiltration therapy shows complete disappearance of the deposit; anasthenous with marked relief of local symptoms.

emphasized that only one large bursa is normally present. Apparently roentgenograms were taken in only a very few cases in this series. Likewise in the article published in 1908 Codman gave paid comparatively little attention to the periarticular deposit. From Codman's case reports it may be surmised that in several patients acute calcified tendinitis might have been overlooked.

Nevertheless, from the findings in Painter's case and in another patient with calcareous deposit which was operated upon by him on May

25, 1908 Codman (1908) made the important observation that the deposit was not in the bursa but beneath its base and in or adjacent to the tendon of the supraspinatus. Although most of Codman's patients were still treated by manipulation under anesthesia, he seemed to favor open operation in selected cases.

In 1911 Codman recorded two more operations in patients with periarticular calcification discovered by roentgenograms. These further substantiated the intratendinous location of the deposit. In one conservatively treated patient inflammation of the bursa was thought to be caused by a "rupture of the web-like sack" into the bursal cavity.

Stueda, in 1908, had regarded the deposit as result of goit of the bursa. At the end of the same year however Bergemann and Stueda found no evidence of one and in 3 patients who had acutely painful shoulders upon which operation had been performed.

Excellent reproductions of the roentgenograms of 6 patients with calcareous deposit of the shoulder were given by Haerwich in 1902. In 1 case excision of the bursa was performed, with recurrence of the deposit. Wrede in 1912 reported an open operation in man 70 years old, in whom he found the deposit in the tendon, but not in the bursa.

A series of shoulders in 8 of which open operation was performed was reported by Brickner in 1917. This investigator likewise stressed the intratendinous location of the deposit. Luk



Fig. 5. Case 26, C. S. Roentgenograms of both knees showing large, irregular bony calcareous deposits (arrows) in the rectus femoris tendon on both sides.



Fig 6 Case 31, K B a, Oblique view of both feet showing normal inconstant second tubal sesamoid (arrow) on the right side (at right) The left second tubal sesamoid (large arrow in left film) is surrounded by calcareous deposits (small arrow), which spread toward the base of the

proximal phalanx b, Special sesamoid technique showing the inconstant second tubal (large arrow) on both sides Note the calcareous deposits (small arrows) around the sesamoid on the left side (film at left)

Codman, Brickner considered that the subacromial and the subdeltoid bursa were one and the same

The results of the pathological examination of the tissue removed by Brickner in 4 cases were presented by Moschcowitz in 1915 He found the lesion to be intratendinous, and thought that "calcification only occurs in dead or inert tissue, that is, tissues that have no blood supply It never occurs in tissues whose blood supply is abundant"

Numerous investigators, including Carnett (1925), Ayzac (1926), Elmsie (1932), and many others, have contributed to our knowledge of acute calcified tendinitis Schaer (1936) published a large work with an extensive bibliographical review Sandstroem and Wahlgren (1937) gave pathological findings in 12 cases in which open operation had been performed Roentgen therapy was used by Sandstroem (1938) with apparently favorable results in a number of cases There was no mention of infiltration treatment

Richards, in 1931, accidentally discovered that intravenous injections of iron cacodylate relieved acute painful shoulders His 3 reported cases are, however, not convincing

The first report of prompt relief of symptoms by aspiration under local anesthesia was that of Flint, of Yale, in 1913 Two patients with acute shoulder lesions were promptly relieved by this treatment In both cases, 3 to 4 cubic centimeters of straw-colored fluid, which was sterile and coagulated on standing, was obtained

A year later, Sievers (1914), in Germany, cognizant of Flint's publication, described the case of another patient similarly treated, with success No roentgenographic findings were given Weeks and Delprat, in 1936, claimed that in 1908 a patient with acute painful shoulder was promptly relieved after aspiration of 2 cubic centimeters of straw-colored fluid They advo-

cated multiple "needling" under local anesthesia, which gave them good results also in cases without calcareous deposit The "needling" treatment has been used successfully by these investigators in additional cases treated after 1933

Haldeman and Soto-Hall, in 1935, referring to cases of acute shoulder lesions, stated that they "have made it a practice to inject from 10 to 15 cubic centimeters of 1 per cent procaine hydrochloride into the bursa" Relief of pain and frequently disappearance of the deposit were obtained within a few days, but repeated injections sometimes were necessary

Treatment of acute subacromial bursitis by open exploration or novocain injection was employed by Haggart and Allen in 1935, who stated "Of the above two methods the most dramatic in its relief is that of exploration and drainage" The injection treatment was first attempted by these workers in 1934 Although favoring the open operation, they admitted that the novocain injection treatment "was strikingly helpful" in all cases of acute bursitis

In 1938 Ferguson wrote that the novocain injection method has come "into favor during the past few years"

Patterson and Darrach, in 1937, described a method of removing the deposit by means of washing the bursa through two needles inserted into its cavity Later, Patterson and Patterson (1940) reported further experience with this method In 2 per cent of their cases general anesthesia was employed Sometimes it was necessary to insert 3 or 4 needles "if a good flow was not obtained between the first two" The authors admitted that their original intention to wash out the deposit was apparently not always successful However, relief was obtained, despite the fact that the "x-rays have sometimes shown apparently the same amount of calcium after the irrigation as before"



TABLE II.—ANALYSIS OF 34 CASES OF TENDINITIS WITH CALCIFICATION AT VARIOUS LOCATIONS

Factor	Site of tendinitis						
	Shoulder	Elbow	Wrist	Hand	Foot	Total	
Number of patients	34	6					
Sex							
Male	23					23	
Female	6					6	
Age in years							
20-25							
26-30							
31-35	2					2	
36-40		2				2	
41 and over	1					1	
Unknown						6	
Side affected							
Right	9				2	11	
Left						20	
Unknown							
Unknown							
History of symptoms							
Acute	12	6	2			20	
Chronic							
Clinical findings							
Localized tenderness	16					16	
Painful and limited motion	13					13	
Muscular atrophy							
Artery changes							
Other symptoms							
Treatment							
Infraction therapy						13	
No infraction therapy	17					17	
Aspiration of calcareous material							
Excisional							
Unexcisional							
Not done	10					10	
Immediate reaction to infraction therapy							
Exacerbation of pain							
No exacerbation of pain	1					1	
Unknown							
X-ray findings after infraction therapy							
Complete disappearance of deposit with clinical cure							
Complete disappearance of deposit without clinical improvement							
No change in deposit with clinical improvement							
No change in deposit and no clinical improvement							
Unknown							
Follow-up							
17	1					1	
17	6					6	

TABLE II—ANALYSIS OF 34 CASES OF TENDINITIS WITH CALCIFICATION AT VARIOUS LOCATIONS  
—Continued

Factor	Site of tendinitis						
	Shoulder	Elbow	Hip	Knee	Wrist	Foot	Total
Follow-up 3 yr	1						1
No one	4	5	3	3	1	4	20
Late results† Excellent	11	1					12
Good	1			1			2
Poor							
Unknown	4 <sup>a</sup>	5 <sup>a</sup>	3 <sup>a</sup>	3 <sup>a</sup>	1 <sup>a</sup>	4	20

\*Acute—severe pain with disability; chronic—occasional pain without disability

†Includes fullness and increased heat over affected area. Trendelenburg sign.

‡Excellent—disappearance of pain within a few days accompanied by gradual disappearance of the deposit and no recurrence of pain on follow up; good—complete and permanent relief of symptoms without complete disappearance of the deposit; poor—persistence of pain and limitation of motion with or without diminution or complete disappearance of the deposit.

§One patient who had tendinitis of the right shoulder to begin with was found on follow up to have occasional pain in the left shoulder also. The right (treated) shoulder was symptomless. X ray showed absence of a deposit in the right shoulder but there was a small deposit in the left supraspinatus tendon.

¶This patient had a spontaneous recovery. Symptoms and deposit gradually disappeared with only physiotherapy.

||No attempt at aspiration was made in 1 case since there was no deposit, although the patient complained of occasional pain for the past 2 or 3 months during bowling. The second case was the patient who recovered spontaneously with only physiotherapy.

¶¶The early result (a few months after infiltration therapy) is known in 2 cases, 1 of which had an excellent result and the other a poor result.

¶¶¶The early result (a few months) is known in these 5 cases. Of 2 receiving infiltration therapy, 1 had a poor early result and the other an excellent immediate result. Of the 3 remaining cases, 1 treated by Dr. M. Burman had a good early result in response to physiotherapy and rest, one courtesy of Dr. H. Sonnenschein had an excellent early result from open operation, and the third courtesy of Dr. A. Kenin had a good early result upon aspiration of the calcareous deposit.

¶¶¶¶One had an excellent early result and 2 had a good early result. Of the latter, 1 was treated by Dr. M. Burman.

¶¶¶¶¶One had a good early result when treated by rest and immobilization and 2 had a poor early result when similarly treated with physiotherapy.

¶¶¶¶¶¶This case courtesy of Dr. Leo Mayer had a poor early result.

¶¶¶¶¶¶¶This patient had calcification in the Achilles tendon. He is an example of a chronic, symptomless intratendinous calcification which was discovered during a general physical examination when a hard rod like, nontender mass was noted in the right Achilles tendon over the place of tenotomy in early childhood. The patient had had mild congenital right clubfoot which had been corrected by open lengthening of the Achilles tendon.

¶¶¶¶¶¶¶¶This patient had tendinitis with calcification in the lumbrical and interosseal tendons of the left second toe, and had an excellent early result 3 months after open operation performed by another surgeon.

calcareous tendinitis because it seems to abort and shorten the acute stage and to prevent recurrences.

The amount of novocain solution and saline used seems to have no direct influence upon the results obtained, except that the solutions should be injected directly into the deposit. It also appears to be more rational to initiate the infiltration with a small amount of novocain followed by a larger amount of warm normal saline, since the latter is less toxic.

#### OBSERVATIONS

Tendinitis with calcification occurs far more frequently at the shoulder joint than in any other part of the body. This is borne out by Sandstroem's series of 329 cases of calcified tendinitis reported in 1938, in which the location of the lesion varied as follows: shoulder, 259 cases, hip, 48 cases, elbow, 6 cases, fingers, 6 cases, knee, 5 cases, toes, 3 cases, and wrist, 2 cases. In the author's series of cases the shoulder also was the most frequently involved.

This may be explained by the evolutionary changes of the shoulder joint and its anatomical and functional peculiarities. The scapulohumeral

articulation in man has the greatest range of motion, as compared with any other joint. This extreme hypermobility is made possible by the great disproportion of the articular facets of the humeral head and the glenoid fossa. The articular surface of the head is four times greater than that of the glenoid fossa (Lanz and Wachsmuth, 1938). The angular value of the vertical arc in frontal plane formed by the glenoid fossa is 75 degrees, while that of the humeral head is 153 degrees (Steindler, 1935). Because of this difference in the articular surfaces, a very large part of the shoulder joint is represented by a joint capsule. According to Fick (1904), the intra-articular space is so great that it can accommodate a "second humeral head." The hypermobility of the arm is further augmented by the movable attachment of the scapula to the thorax.

In the horizontal posture of quadrupeds, both the front and hind legs are designed to bear the weight of the body, and the humeral head is pressed against the glenoid fossa in a manner similar to the femoral head bearing against the acetabulum. With the adaption of upright posture, the upper limb became suspended from the body. The weight of the arm itself tended to

separate the humeral head from the glenoid fossa. This was prevented by the joint capsule and the muscles, both of which were under tensile load in an upright position. Some of the muscles, especially the supraspinatus, are comparatively weak and inadequately adapted for the new mechanical requirements, because of the relatively recent adaption of upright posture. As stated by Codman, it became necessary for "the supraspinatus to lift the arm instead of swinging the forearm." Lifting any weight especially with the arm in frontal abduction, puts a tremendous tensile load on the capsule and muscles acting against great leverage.

As pointed out by Duplay, the shoulder joint is the only one in which in addition to the intra capsular motion, there is a mobility between the capsule of the acapulohumeral articulation and the socket formed by the acromion and the coracoclavicular ligament. The large subacromial bursa and the loose subdeltoid areolar tissue help to produce free gliding motion in this "second shoulder joint." Although most of the time the joint capsule and the periarthicular soft structures are subjected to tension, occasionally there is relaxation to the permissive mechanical condition. For instance, when something is pushed with the hand or when one falls forward on the out stretched hand, an upward thrust is produced, pressing the head of the humerus against the glenoid fossa and at the same time compressing the upper part of the joint capsule between the rigid socket of the "second shoulder joint" and the head of the humerus. This probably is the reason why the tendinous cuff of the shoulder joint especially the uppermost supraspinatus tendon, is subjected to continuous mild traumatization or acute severe injury resulting in degenerative changes with calcification or tendinous tears, respectively. It is doubtful that trauma may be immediately followed by formation of a calcareous deposit. Most probably it takes weeks, and possibly months, for calcification to take place. However a latent deposit, whether of post traumatic or other origin may be activated by a recent injury to produce symptoms and disability in an apparently healthy individual.

In addition to trauma, there may be some metabolic predisposition of the individual toward calcification. This is evident from the fact that the deposit is rarely observed in young persons. The far greater frequency of involvement of the right shoulder noted in all reviewed papers indicates trauma as one of the etiological factors.

It is obvious that although tendinitis with calcification occurs most frequently at the shoulder

it is by no means restricted to this location. The elbow, hip, knee, foot, and wrist have been involved in the author's series, as well as in cases reported in other publications. There is a close resemblance between the lesion at the shoulder and that at the hip due to homology of these two joints.

The infiltration therapy has been found to be successful in these different locations in acute cases. The author is fully aware of the possibility of the occurrence of spontaneous recovery with complete disappearance of the deposit in patients with acute calcareous tendinitis. Nevertheless, his observations have convinced him of a definite benefit from the infiltration therapy in acute cases. Relief of pain is often dramatic and, as a rule, is followed by disappearance of the deposit.

#### SUMMARY

1. Acute tendinitis with calcification most commonly occurs at the shoulder joint, although this lesion may be located in other parts of the body.

2. The infiltration therapy of acute tendinitis with calcification has given quite satisfactory results in the series of cases presented, with few exceptions. Treatment is accompanied by relief of pain after initial exacerbation of symptoms, and by gradual disappearance of the deposit.

3. In cases of "frozen shoulder" the infiltration treatment was found to be of no value while in chronic cases with mild symptoms its effect is doubtful.

#### REFERENCES

1. AYUD, C. Les calcifications des bourses séreuses périarticulaires. Thèse Faculté de Médecine de Paris, 1925, No. 57.
2. BLEIBERGER and STEIN, A. *Möck med. Woch.* 1928, 55: 2699-2702.
3. BRIDGES, W. M. *J. Am. M. Ass.* 9: 76 57-84.
4. CANNETT, J. B. *Surg. Gyn. Obst.* 9: 54 404-41.
5. COMEAU, E. A. *Boston M. & S. J.* 1904, 30: 37 374.
6. *Ibid.* 1905, 31: 6 3-620.
7. *Ibid.* 1905, 31: 533-537.
8. *Ibid.* 1905, 31: 5-120.
9. *Ibid.* The Shoulder. Boston: Thomas Todd Co. 1934.
10. COVIELL. Quoted by *Jama* 7: 11 J F 267.
11. *DEER* 1922, 11: *Gas. Med.* 375, 374-375.
12. DUPLAY, S. *Arch. gén. méd.* 874, 518-542.
13. ELMORE, R. C. *Bell. J. Surg.* 912, 20 100-106.
14. FERGUSON, L. K. *Surg. Gyn. Obst.* (Internat. Abstr. Surg.) 1915, 64: 473-57.
15. FICK, R. *Handbuch der Anatomie und Mechanik der Gelenke*. Vol. 1. Jena 1904, p. 7.
16. FLETCHER, J. M. *J. Am. M. Ass.* 9: 3, 60 31 35.
17. HARNACK, G. F. *Fortsch. Röntgenstrahl.* 9: 2, 3 203-200.
18. HANCOCK, G. F. and ALLAN, H. A. *Surg. Clin. N. America*, 1935, 5: 537-550.

- 19 HALDEMAN, K O, and SOTO HALL, R. J Am M  
Ass, 1935, 104 2319-2324.
- 20 JARJAVAY, M J F Gaz hebd, 1867, 4 325-327,  
357-359, 387-391
- 21 LANZ, T, VON, and WACHSMUTH, W Praktische  
Anatomie Vol 1, part 4, p 96 Berlin Julius  
Springer, 1938
- 22 LERICHE, R., and JUNG, A Rev chir, Par, 1938, 76  
382-385
- 23 MILGRAM, J E Personal communication
- 24 MOSCHCOWITZ, E Am J M Sc, 1915, 150 115-126
- 25 PAINTER, C F Boston M & S J, 1907, 156 345-349
- 26 PATTERSON, R L, JR., and DARRACH, W J Bone  
Surg, 1937, 19 993-1002
- 27 PATTERSON, R. L, JR., and PATTERSON, R H Am J  
Surg, 1940, 49 403-408
- 28 POURTIN (1902) Quoted by Ayzac, C, 1926
- 29 PUTNAM, J J Boston M & S J, 1882, 107 509-512,  
536-539
- 30 RICHARDS, T K N England J M, 1931, 205 812-  
813
- 31 ROGERS, M Am J Surg, 1939, 43 292-297
- 32 SANDSTROEM, C Am J Roentg, 1938, 40 1-21
- 33 SANDSTROEM, C, and WAHLGREN, F Acta radiol,  
1937, 18 263-296
34. SCHAEER, H Erg Chir Orthop, 1936, 29 211-309
- 35 SIEVERS, R Deut. Zschr Chir, 1914, 129 583-653
- 36 STEINDLER, A. Mechanics of Normal and Patho-  
logical Motion in Man P 290 Springfield, Illinois  
Charles C Thomas, 1935
- 37 STIEDA, A Arch klin Chir, 1908, 85 910-924.
- 38 WEEKS, A, and DELPRAT, G D Internat. Clin, 1936,  
3 40-48
- 39 WREDE, L Arch klin Chir, 1912, 99 259-279

# THE INHIBITORY EFFECT OF PROCAINE ON THE BACTERIOSTATIC ACTIVITY OF SULFATHIAZOLE

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THE increasing use of the sulfonamide drugs in the treatment of traumatic wounds has aroused considerable speculation as to the mechanism of their action and the factors which influence their activity. Since the report of Jensen and his co-workers on the treatment of compound fractures, surgeons have advocated the topical application of one of the sulfonamide drugs in a variety of infected or potentially infected wounds. That no ill effects have resulted from this use has been demonstrated by the work of Tuffe and Harvey, Key and Frankel, and others, although Bricker and Graham noted some inhibition of wound healing following the local application of sulfanilamide crystals.

The action of the sulfonamides is bacteriostatic rather than bacteriocidal and the various drugs in this group exhibit a selective activity toward different pathogenic organisms. Furthermore, certain conditions may prevent completely or inhibit their bacteriostatic activity. Lockwood (5, 6, 7) has shown that small amounts of peptone and peptone-like substances in culture media inhibit the activity of sulfanilamide. Strauss and Finland detected a selective inhibition of sulfonamide drugs by media of blood, both human and horse serum, and liver infusion medium.

Spink and Jernsta have studied the *in vitro* effect of para-amino-benzoic acid on the bacteriostatic activity of sulfathiazole against *Staphylococcus aureus* and found that a definite inhibition of this activity occurred. Similar results were obtained by McCarty and by Ketch, Baker, Knafl, and Clowes, who worked with the various local anesthetics derived from para-amino-benzoic acid. The latter group observed that a definite antagonistic effect was exerted by these derivatives on the activity of sulfathiazole in solutions inoculated with *Staphylococcus aureus* and *Bacillus coli*.

The clinical applications of this experimental work are well worth considering. A study of the bacteriology of infected and traumatic wounds by Longmire revealed that the staphylococcus was an

almost invariable inhabitant. The use of local anesthetics in the treatment of compound fractures and other traumatic and potentially infected wounds is widespread, and the anesthetic in most common use is probably procaine (N diethylamino ethyl para-amino-benzoate), a derivative of para-amino-benzoic acid. If this compound exerts the same inhibitory effect on sulfathiazole *in vivo* that it does *in vitro* the present method of treatment may have to be revised.

A report of our experimental attempts to ascertain the occurrence of this phenomenon follows. Of course, it is realized that it is extremely difficult to produce experimentally a wound that is exactly analogous to the traumatic wound. In the latter while the number of organisms may be low, the variety is greater and frequently according to Meleney anaerobic bacteria may be present or the various organisms present may have a synergistic effect which pure cultures do not have. Furthermore the nature of the traumatizing agent is usually quite dissimilar. However since the *Staphylococcus aureus* is an almost constant inhabitant and is known definitely to be pathogenic, the experimental work was carried out on wounds inoculated with this organism.

## METHODS OF STUDY

In these studies sulfathiazole was the only sulfonamide utilized. This drug is probably the one of choice for use in traumatic wounds because of its action on the almost constantly present staphylococcus and because of its relatively slow absorption. The infecting organism used was a strain of *Staphylococcus aureus* from a case of acute osteomyelitis (supplied by Dr. John E. Blair, bacteriologist, Hospital for Joint Diseases) which was known to produce a toxin. This was grown on brain-heart infusion agar for 24 hours and just before use each slant was washed off with 1.5 cubic centimeters of heart infusion broth. One slant was used for each wound. Preliminary experiments revealed that this method produced a local infection in every wound.

Rabbits weighing about 5 pounds (2.3 kilograms) were used in all experiments. Three days before operations the skin of the back was depil-

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lated with barium sulfide. Anesthesia was induced by the intravenous administration of nembutal at the rate of 0.2 cubic centimeter per pound into the ear vein. The average dose per rabbit was 1 cubic centimeter. An incision about 1.5 to 2 inches long was made through the skin of the back, parallel to the spine and about 1 inch lateral and just caudad to the origin of the last rib. This was carried through the fascia, and the sacrospinalis muscle was exposed. By blunt dissection, the fibers of the muscle were separated and a small space was formed. Hemostats were applied to the muscle fibers surrounding the area and the muscle tissue was crushed to simulate as closely as possible the traumatic wound. Three series of experiments were carried out on these wounds. In series I the traumatized muscle wound was inoculated with the suspension of *Staphylococcus aureus* prepared as described previously. The wound was then closed with fine silk. In series II inoculation with the bacterial suspension was similarly performed and then 10 grains (0.65 gm.) of sulfathiazole powder was sprinkled into the wound. Previous experiments in which a smaller amount of sulfathiazole (0.35 gm. and 0.5 gm.) was used demonstrated that the smaller amounts of the drug were ineffective in inhibiting the infection. In series III the skin incision was made as above. The fascia was then infiltrated over an area of 1½ inches with 1 cubic centimeter of a solution of 2 per cent procaine and then incised. The muscle was infiltrated with 2 cubic centimeters of the same solution, and then the fibers were bluntly separated and crushed as in the previous experiments. The wounds were inoculated and the sulfathiazole was inserted as in the other groups. The wounds were likewise closed with fine silk.

All animals were observed for a period of at least 6 weeks following the operative procedures.

#### RESULTS

**Series I** Twelve rabbits. All incisions became infected and definite abscess formation occurred within 2 weeks. The abscesses were thick walled and filled with a heavy purulent secretion. Cultures taken from the abscess cavities yielded *Staphylococcus aureus*.

**Series II** Thirty-three rabbits. In 20 animals no gross evidence of infection was discernible during the period of observation (4 to 6 weeks). The wounds healed *per primam* and, except for a slightly increased amount of thickening, they differed in no way from healed noninfected wounds. The thickening was probably due to remnants of unabsorbed sulfathiazole powder.

TABLE I—INCIDENCE OF INFECTIONS IN VARIOUS GROUPS

	Infection		No infection	
	Number	Per cent	Number	Per cent
Series I—wounds inoculated with <i>Staphylococcus aureus</i>	12	100	0	
Series II—wounds inoculated with <i>Staphylococcus aureus</i> and 0.67 gm of sulfathiazole	13	39.3	20	60.6
Series III—wounds inoculated with <i>Staphylococcus aureus</i> and 0.67 gm of sulfathiazole and infiltrated with 3 c.c. of 2 per cent procaine	26	100	0	

Several of the wounds were incised again after 2 or 3 weeks and cultures were taken. In all cases a staphylococcus was obtained corresponding to the infecting organism. This would lend support to the contention that the action of sulfathiazole is bacteriostatic rather than bacteriocidal. A delayed infection or an attenuated type of infection was observed in 8 rabbits. In these, the infection either developed very slowly as compared to the 2 week period in series I, or appeared in a much milder form. In the latter, no definite abscesses were observed but rather a diffuse infection with dehiscence of the wound and purulent drainage around the suture openings. In the animals with delayed infection a slowly developing induration and edema were observed for 7 to 14 days, and this was followed by breaking down of the wound and extrusion of small clumps of sulfathiazole powder and purulent material. Sections of the wounds revealed a true inflammatory process involving skin, muscle, and fascia. Finally, in 5 rabbits, definite abscesses developed within 2 weeks and were completely identical with those in series I.

**Series III** Twenty-six rabbits. Definite abscesses developed in all animals. In several, the appearance was slightly delayed beyond the 2 week period observed in series I, but in no case was this delay beyond 3 weeks. The abscesses were fairly large and well localized. Occasionally the edges of the incisions separated but in a majority of the animals good healing of the skin and subcutaneous layers was observed.

#### ANALYSIS OF RESULTS

The studies heretofore described offer fairly definite experimental evidence that procaine, in the dilution and quantity used, will inhibit or entirely prevent the bacteriostatic activity of sulfathiazole in wounds infected, at the time of trauma, with a suspension of *Staphylococcus au-*

reus. Statistical analysis of these results demonstrates a significant difference between the percentage of infections in series II and series III. In the former only 39.3 per cent of the wounds became infected, including those with slight or delayed infections, while in the latter 100 per cent developed abscesses. If we were to exclude those animals in series II in which the infection was minimal, the percentage difference would be even more striking. On the basis of these experiments, however one cannot state that procaine would always be 100 per cent effective in inhibiting the activity of sulfathiazole because, according to the laws of probability one might still get infections in each of a group of 26 rabbits if procaine was only 84 per cent effective. We can be certain, however, that in groups similarly treated (series III) not less than 84 per cent of the animals would develop an infection. This figure (84 per cent) when compared to the 39 per cent of series II is still significantly different and therefore, the results reported are definitely not due to chance alone. This statistical corroboration is essential in all work of this nature in order to eliminate the effect of chance variations, and to make certain that the numerical composition of each group is adequate for the conclusions drawn from the experimental results.

Sulfathiazole, therefore may be said to prevent infection in experimentally infected wounds (*Staphylococcus aureus*) in approximately 60 per cent of the cases. The addition of 2 per cent procaine solution in amounts ordinarily used clinically will diminish this effectiveness considerably. In the present series it was 100 per cent effective in eliminating the bacteriostatic action of sulfathiazole, and from the standpoint of statistical evaluation, we may state that it will be at least 84 per cent effective in all similar groups.

The clinical application of these studies is evident. While procaine was the only derivative of para-amino-benzoic acid studied, the results of *in vitro* experiments would lead one to believe that other anesthetic agents derived from this chemical, would behave similarly *in vivo* (3, 14). Therefore in the treatment of infected or potentially

infected wounds, it would seem advisable to forego the use of local anesthesia, or if this is impossible, to employ larger amounts of sulfathiazole and use greater dilutions of the anesthetic agent.

#### SUMMARY AND CONCLUSIONS

1. The bacteriostatic action of sulfathiazole can be inhibited *in vivo* by many agents. Para-amino-benzoic acid and its derivatives are among the most potent of these inhibitors.

2. Many local anesthetic agents in common use are derived from para-amino-benzoic acid. Procaine (N-diethylamino ethyl para-amino-benzoate) is probably the local anesthetic used most frequently.

3. The experimental work reported herein has shown conclusively that procaine will inhibit the bacteriostatic activity of sulfathiazole in wounds inoculated at the time of trauma with a suspension of *Staphylococcus aureus*.

4. As a result of these studies we are of the opinion that the use of procaine for local anesthesia in the treatment of compound fractures and traumatic wounds is contraindicated when sulfathiazole is to be applied topically.

#### REFERENCES

- BRIDGES, E. and GRABER, E. A. *J. Am. M. Ass.* 930, 293.
- JONES, N. K., JOURNARD, L. W. and NELSON, M. C. *Surgery* 930, 61.
- KELTON, A. L., BUELL, L. A., KRAHL, M. E., and CROWER, C. H. A. *Proc. Soc. Exp. Biol.* N. Y. 94, 47, 533.
- KRY, J. A., and FRANKEL, C. J. *Arch. Surg.* 1941, 534.
- LOCKWOOD, J. B. *Surgery* 94, 493.
- Idem. *Ann. Surg.* 94, 108, 109.
- Idem. *Surg. Gyn. Obst.* 94, 307.
- LOWACREY, A. B. *Surg. Clin. N. America*, 94, 31, 377.
- McCAFFERTY, M. *Proc. Soc. Exp. Biol.* N. Y. 1941, 40, 33.
- McKENNEY, F. L. Discussion of paper of Kry and Frankel, loc. cit.
- SMITH, W. W. and JENNISTA, J. *Proc. Soc. Exp. Biol.* N. Y. 1941, 47, 305.
- STRAUSS, E., and FIDLAND, M. *Proc. Soc. Exp. Biol.* N. Y. 94, 47, 490.
- TARTEL, M., and HARVEY, S. C. *Proc. Soc. Exp. Biol.* N. Y. 94, 47, 502.
- WOODS, D. D. *Brit. J. Exp. Path.* 1940, 74.

# EVALUATION OF DYSMENORRHEA BY BASAL BODY TEMPERATURE

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**P**ROLIFERATIVE as well as progestational premenstrual endometrium have been associated with dysmenorrhea by Hirst, Hamblen, and Cuyler. On the other hand, Wilson and Kurzrok observed secretory endometrium premenstrually in each instance of essential dysmenorrhea which they studied. They furthermore produced dysmenorrhea in an amenorrheic individual by means of progesterone. They concluded that only women with corpus luteum function can have dysmenorrhea. Sturgis and Albright (11) noted that dysmenorrhea did not occur in the absence of a secretory endometrium, thus tending to confirm the original observation by Wilson and Kurzrok. This association of ovulation and anovulation with dysmenorrhea seems to merit further examination.

It is the purpose of this presentation to investigate the contention, by means of the basal temperature approach, that ovulation is prerequisite to dysmenorrhea. Basal body temperatures of women, contrary to men, fluctuate during the month (6). Basal temperatures have been used by Rubenstein (7), A. Palmer (4), R. Palmer (5), Vollmann, and Zuck to indicate ovulation. Use is made of the sharp rise in basal temperature in the progestational phase of the ovulatory cycle. Such an alteration does not occur in the anovulatory cycle, so the temperature remains essentially unchanged throughout. However, the daily fluctuations may be relatively wide in range.

Vollmann observed that the duration of the premenstrual phase was relatively independent of the length of the menstrual cycle. On the other hand the duration of the postmenstrual phase varied directly with the cycle length. Rubenstein (8) plotted the zenith of cyclic basal temperatures at 5 to 10 days premenstrum, whereas the nadir averaged 15 days prior to menstruation.

Correlations between basal temperature and vaginal smear techniques were demonstrated by Rubenstein and Lindsley (9) during 5 menstrual cycles. Rubenstein concluded that the temperature cycle was as reliable an indicator of ovulation

as the vaginal smear. There was established a +93 correlation between the low point of the basal temperature curve and a smear typical of maximal estrone activity. This same author later (8) made use of the basal temperature for determination of ovarian function for which it was considered a better criterion than the vaginal smear.

Palmer and Devillers observed the effect of estrogen, progesterone, and testosterone on ovariectomized women in regard to basal temperature. Estrogens and testosterone produced a decrement in thermal level whereas progesterone caused an increase. Wertenberger, Collet, and Smith confirmed the fall in temperature during estrogen administration. A. Palmer (4) believes that the rises and falls are produced by activity of the ovarian hormones. By means of endometrial biopsy correlation, he concluded that the progestational phase of the normal ovarian cycle is relatively constant and averages 14 days in length regardless of the length of the cycle. He saw no exceptions to the correlation of basal temperature with the microscopic endometrial picture.

Barnes has suggested that temperature taken under basal conditions reflects the metabolic level. Progesterone utilization in physiologically effective amounts appears to raise the metabolism. This can be demonstrated upon progesterone administration to anovulatory women. It further appears that basal temperatures reflect the increase of metabolism occurring during progestation. Ovulation is, of course, a prerequisite to this state of affairs.

Sturgis (10) has recently defined essential dysmenorrhea as menstrual cramps associated with the presence of a secretory endometrium. He suggested the diagnostic differentiation between recurrent abdominal pain of other types and that of dysmenorrhea by means of inhibiting the secretory or progestational phase of the cycle, and claimed that the true dysmenorrhea can consistently and fully be prevented by estrogenic therapy. From these considerations it is clear that the basal temperature in women follows variation in the ovarian activity and reflects the progestational phase of ovulatory cycles. Therefore, it seems desirable to determine the basal temperature conditions in dysmenorrhea.

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This study was assisted by the Christine Breon Fund for Medical Investigation.



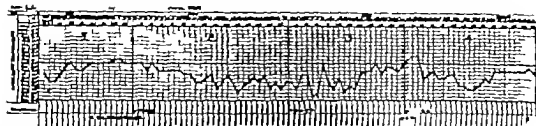


Fig. 1. Basal body temperature of successive cycles to include anovulation between two ovulatory cycles in an instance of primary dysmenorrhea. C, Symbolizes dysmenorrheic cramps. ( ) Basal temperature increased during preovulatory phase of cycle suggesting ovulation. Cramps

are present. ( ) Apical temperature occurred anovulatory cycle. Cramps were absent. ( ) Biphasic basal temperature suggested ovulation. Cramps were present. ( ) Ovulation again occurred, and cramps were again present.

#### OBSERVATIONS

Thirty dysmenorrheic women have been observed by means of basal temperature curves taken daily over a period of at least 3 months. One hundred and twenty-seven cycles have been studied. The patients ranged in age from 16 to 34 years, with an average age of 26 years.

Eighteen of the group had endometrial biopsy specimens taken late in the cycle. All of them had preovulatory endometria and all were associated with a premenstrual elevation in temperature. Furthermore in 4 patients observed for more than 6 months each sporadic anovulation as determined by basal temperatures was not accompanied by recurrent crampy pain.

Endometrial biopsy samples were obtained by the Novak curette between the 24th day of the cycle and the 1st day of the new cycle. They were also taken during the absence of ovulation. This resembled the picture seen in such conditions as hyperplasia of the endometrium or during lactation, and in simple gonadotropic anovulation. The endometrial pattern shows no progesterone, and there is ordinarily no phase of temperature increment. In such instances the stroma retains a dense cellular appearance and the uterine glands maintain their early proliferative pattern. In these instances of anovulation, there was no attendant pain of the dysmenorrheic type.

Endometrial samples from the dysmenorrheic patients here discussed showed reticulated loose stroma and wavy uterine glands representative of progesterone in each patient examined. Although the incidence of anovulation in healthy young women is low slightly less than 5 per cent as cited by Morton and Hayden, each instance of dysmenorrhea observed was accompanied by a temperature curve showing relatively high readings during the last half of the cycle.

Figure 1 presents the basal temperature record of one anovulatory painless 30 day cycle between

two ovulatory cycles, both of which are accompanied by recurrent pain. The cycles represent the presence of late cyclic preovulatory metabolist rise in ovulatory cycles and its absence in the anovulatory cycle record.

#### CONCLUSION

It appears from this study that dysmenorrhea is associated with a temperature curve which has as its common factor the characteristic of late cyclic elevation associated with ovulation. When, for one reason or another the cycle is anovulatory there is no dysmenorrhea. Evidence is adduced in support of Hime's contention that dysmenorrhea may occur in the presence of proliferative endometrium.

Anovulatory cycles as determined by either basal temperature records or endometrial biopsy were not associated with dysmenorrheic pain. Conversely each episode of dysmenorrhea was associated with the characteristic temperature curve, typical of ovulation.

#### SUMMARY

One hundred and twenty-seven dysmenorrheic cycles have been followed in 30 women of age range 16 to 34 years. Preovulatory temperature rise occurred in the last half of the cycle in each instance of dysmenorrhea in each cycle in which dysmenorrhea occurs. Anovulation was not associated with dysmenorrhea. Basal temperatures appear to assist in the differentiation of essential dysmenorrhea from their rhythmical pains which may be associated with menstruation. This is confirmatory evidence by the basal temperature method of the regular precedence of ovulation in essential dysmenorrhea.

#### REFERENCES

1. BAKER, B. *J Am Med Ass* 942, 20, 773
2. HIME, D. V., HANDEL, E. C. and CUTLER, W. R. *J Clin Endocr* 942, 442

- 3 MORTON, D G, and HAYDEN, C T West J Surg, 1941, 49 15
- 4 PALMER, A Surg Gyn Obst, 1942, 75 768
- 5 PALMER, R, and DEVILLERS, J C rend Soc biol, 1939, 130 805
- 6 RUBENSTEIN, B B Am J Physiol, 1937, 119 635
- 7 Idem Endocrinology, 1940, 27 843
- 8 Ibid, 1938, 22 41
- 9 RUBENSTEIN, B B, and LINDSLEY, D B Proc Soc Exp Biol, N Y, 1937, 35 618
- 10 STURGIS, S H N England J M, 1942, 226 371
- 11 STURGIS, S H, and ALBRIGHT, F Endocrinology, 1940, 26 68
- 12 VOLLMANN, U Mschr Geburtsh Gyn, 1940, 111 41, 121
- 13 WERTENBERGER, G L, COLLIER, M E, and SMITH, J T Am J Physiol, 1936, 116 159
- 14 WILSON, L, and KURZROK, R Endocrinology, 1938, 23 79
- 15 ZUCK, T T Am J Obst, N Y, 1938, 36 998

## IMMEDIATE ACTIVE MOTION TREATMENT OF FRACTURES OF THE HEAD AND NECK OF THE RADIUS

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A SURVEY of the literature concerning the treatment of fractures of the head and the neck of the radius indicates that there is great controversy as to whether conservative treatment with immobilization or radical treatment with the removal of the head of the radius is better. The very fact that such a controversy exists is indicative that either treatment leaves much to be desired as far as the restoration of normal function is concerned. This, too, is clearly brought out by the reports of the results obtained in various series of cases. With this in mind, this report presents a series of unselected cases of fractures of the head and neck of the radius treated by a third method, that is, the immediate use of active motion and local heat with no immobilization other than the use of a simple arm sling. Perusal of the literature reveals only two other instances in which early active motion is advocated. One instance is that of a report by Colp who advocates immediate resection of the head in all cases, irrespective of the amount of displacement with immediate active motion after operation. The other is that of a recent report by Neuwirth dealing with 6 cases of varying types of elbow fracture which were treated successfully with immediate active motion.

### ESSENTIAL ANATOMY

In discussing the rationale of this treatment, it is necessary to consider certain anatomical features of the elbow joint. The elbow joint is unique in the body, being a bicondylar joint with the

humerus articulating with the ulna and the radius, and also with the close approximation and relation between the proximal ends of the radius and ulna. The two condylar joints do not have the same axis, nor do they move through the same arc. Consequently, in order for a normal range of flexion and extension to be present, these 2 joints must be perfectly synchronized. Therefore, any anatomical variation disturbing the axis or arc of either of these joints will produce some degree of mechanical block. Cohn states that "any change in the axis of an articular surface is bound to produce a partial or complete ankylosis of the joint." It follows, therefore, that reduction of the fragments of a fractured elbow may eliminate any obvious deformity but still not restore the state of synchronization of the two condylar joints, with appreciable impairment of function resulting. Furthermore, x-ray evidence has not proved an accurate guide as to whether the position of the fragments is normal anatomically, and, therefore, fixation until calcification has occurred will succeed in nothing except to insure that synchronization is lost and bony blocking of the joint motion will result. The massage, active and passive motion, and other routine physical measures employed for the restoration of function will not only be unavailing but may even do further damage in that injudicious attempts to increase the range of motion by these methods may compress the articular cartilage, initiate a hypertrophic arthritis, or produce a hematoma that may rapidly ossify.

The head of the radius has two important functions—one is its articulation with the ulna to form

the proximal radioulnar joint through which rotation of the forearm is executed, and the second is its rôle in maintaining lateral stability of the elbow joint. The close relationship of the radial head to the ulna is an important consideration since exuberant callus formation may ankylose the proximal radioulnar joint, thereby impairing rotation of the forearm.

#### CONVENTIONAL TREATMENT

After the presence of a fracture is established the question of treatment arises. In general, conservative treatment is used in fractures with little or no displacement, and resection of the uncontrollable capital fragment is employed in fractures with gross displacement. That neither method is particularly satisfactory is obvious from the reports and opinions of various authors. Eliason and North conclude that "in none of these cases should too optimistic a prognosis be given, for traumatic arthritis with painful restrictive rotation may follow an apparently minor injury with or without displacement and regardless of treatment."

Bohrer in a report on 20 cases, 15 of which were treated conservatively and 5 by resection of the head of the radius, concludes that both methods result in appreciable loss of function, especially due to synostosis of the radius and ulna, producing loss of rotation. Callus formation may produce this after operation, as well as with conservative treatment. Synostosis due to exuberant callus occurred in 50 per cent of the 8 patients operated upon in his series. With the 12 patients treated conservatively the results were consistent with the amount of displacement.

Schwartz and Young report a series of cases treated conservatively in which all showed some disability although in the cases with little or no displacement, functional results were adequate. These authors are opposed to resection of the head of the radius, stating that this structure is essential for the stability of the elbow joint, and that its removal produces relative lateral instability. Cobbins, Callahan, and Scuderi concur with this observation, as also does Magnusson.

King reports a series of 13 cases, all treated with early resection of the head. He considered 1 result excellent, 5, good, 4, fair and 3, poor. These figures indicate that there was some disability in all but 1 of the cases, and that in over 50 per cent of the cases there was appreciable disability. The author states that "in too many instances of resection, it is taken for granted that the procedure is harmless and free from undesirable sequelae."

Helm analyzes the end-results of 52 cases, with special reference to disability. Fractures with

little or no displacement were treated conservatively; those with great displacement were treated surgically. In group 1 consisting of 25 cases with no displacement and treated conservatively there were 21 normal results. In group 2 consisting of 11 cases with displacement and treated conservatively 8 had limited extension, 5 had limited flexion, and 4 were chronically painful. In group 3 consisting of 11 cases with displacement and treated with early resection, good functional results were obtained generally but some disability ensued in all cases. In group 4, consisting of 5 cases with displacement and treated with late resection, all had marked decrease in flexion and extension, 4 had marked limitation of both pronation and supination, 1 had complete loss of rotation and 3 were chronically painful. The average time lost was as follows: group 1, 4.66 weeks of disability; group 2, 10 weeks; group 3, 8.5 weeks, and group 4, 23 weeks.

#### RATIONALE OF ACTIVE MOTION TREATMENT

The review given of series of cases reported certainly does not indicate an especially satisfactory result in the conventional conservative treatment. Eliason (5) states "function is to be striven for at the expense of anatomical alignment." He further states in another paper (6) that "after an injury to the elbow the restoration of normal function requires the preservation of the contours and relationships of its several articulating surfaces. The conventionally accepted premise of the conservative treatment of these fractures has, therefore, been based on an attempt to restore anatomically the articular surfaces to as nearly normal as possible, and then to use some method of fixation until the fragments are sufficiently callused to warrant motion without too much possibility of further displacement. However it is possible that a different premise is more acceptable, at least in the cases under discussion: at this time, namely fractures of the head and neck of the radius, because we are dealing with small uncontrollable fragments, the even minute displacement of which may destroy the synchondralization of the multiple articular surfaces of the elbow. As a corollary there is a logical rationale for the nonfixation treatment in fractures of the head of the radius. The fundamental fact to keep in mind is that these fragments are small and uncontrollable. By beginning active motion of the elbow early before the fragments have become fixed, they will be moved across the fixed, uninjured articular surfaces of the humerus, and will thus attain the best functional position in relation to the various joint surfaces."

Under this management, no fixation of the elbow is used other than a simple arm sling holding the elbow at a right angle, this being as nearly a neutral position for the elbow as possible. Continuous hot wet packs are used for as long as is necessary to treat the soft tissue injury and to overcome muscle spasm. Morning and evening the elbow is guided gently by the physician through its range of active motion, extension and flexion being performed with the forearm in supination and an attempt being made to have the patient balance the range of flexion with equal range of motion in extension. Then the forearm is actively moved through its range of supination and pronation. It is to be emphasized that the patient himself is performing the motion, merely supported and guided by the physician, and that at no time is any forceful passive motion used under this management of the early injury. If this procedure is carried out carefully, it is rarely necessary to use any degree of passive force, and that only after the third week of treatment and in the exceptionally unco-operative patient, and then only with great care and the exertion of minimum force.

Additional advantages gained by this method of treatment are the improvement of circulation to the injured area which minimizes the amount of soft tissue scarring and the reduction of degree of scar tissue contracture. Also close observation of the injured member is possible from the outset, permitting early recognition of any complications, such as nerve damage, or such an unfortunate sequela as von Volkmann's ischemic contracture, and would permit early treatment being instituted in such cases.

#### CLASSIFICATION OF CASES

Between May 18, 1941, and August 13, 1942, there were admitted to the Station Hospital, Camp Joseph T. Robinson, Arkansas, 25 patients with fracture of the head of the radius. Seven of these patients (group 1) were admitted prior to April 1, 1942, and were treated by the conventional type of management. Eighteen were admitted after April 1, 1942 (group 2) and have all received the nonfixation, local heat, and active motion type of management.

In attempting to evaluate the results, the following classification was used:

*Class A* Linear, transverse fractures of the head, without displacement, and transverse and impacted fractures of the neck without displacement. This group would, under the conventional management, receive fixation for varying periods, from 10 to 30 days, followed by physiotherapy.

*Class B* Comminuted fractures of the head without displacement or with minimal displacement. This group would conventionally be treated conservatively with longer periods of fixation, with the possibility of subsequent excision of the head of the radius if functional results should prove unsatisfactory. Into class B were placed also fractures of the class A type that were complicated by complete dislocation of the elbow at the time of injury, as it was found that this group was slower in regaining function because of the extensive soft tissue damage.

*Class C* Comminuted fractures with marked displacement. These are generally operated upon early with excision of the head of the radius.

*Class D* Transverse fractures of the neck with displacement of the head, which is often found rotated 90 degrees more or less from its normal longitudinal axis. These patients also require early operation with either replacement or excision of the head as the case may require.

In this series there were no patients coming under class D. There was only 1 patient that fell into class C, and he was transferred to an army general hospital where operation was performed, however, an opportunity to follow and examine him subsequently permits the inclusion of this patient in the series. Under class B there were 3 in the conventionally managed group and 7 in the recent group, making a total of 10 patients. In class A there were 3 in the first group, and 11 in the subsequent group, making a total of 14 patients. It is, therefore, obvious that any conclusion which may be drawn from this series can be applied only to the types of fractures of the head and neck of the radius classified under class A and class B.

No attempt will be made to discuss the incidence, etiology, or to further elaborate upon the pathology in these cases, as the primary object of this discussion is to compare the results obtained under the two types of management outlined above.

#### HOSPITALIZATION PERIOD

In considering the series from the standpoint of period of hospitalization, one must remember that a distinct difference exists between the period of hospitalization in an army hospital and that in a civilian hospital. The former is longer because the patient remains in the hospital until he is capable of performing full duty, whereas the same patient in civilian life would probably be hospitalized only 10 days or 2 weeks and then be returned home for further outpatient care and convalescence. One patient presents an example

TABLE I.—HOSPITALIZATION

Group			
Class A		Class B	
Case No.	No. of days	Case No.	No. of days
	37		85
5	44		12
6	198		118+
Average	93	Average	107+

Group			
Class A		Class B	
Case No.	No. of days	Case No.	No. of days
	42	8	49
10			37
3			28
47		15	36
14		19	31
16	26		39
	30		40
20	51	Average	31
21	45		
24	42		
25	33		
Average	36		

TABLE II.—FUNCTIONAL RESULTS

Group					
Class A			Class B		
Case No.	End result per cent	Days	Case No.	End result per cent	Days
	100	37		50	35
	100	44		50	
6	70	198		50	118
Average	90	9	Average	71.4	100

Group					
Class A			Class B		
Case No.	End result per cent	Days	Case No.	End result per cent	Days
	100	44	8	100	49
10	100			100	37
	100	37	1	100	
	100	44	15	100	36
14	100	33	19	100	31
16	100	25	21	95	39
	100	30		95	40
20	100	49	Average	98	35
21	100	45			
24	100	42			
	100	33			
Average	100	30			

of how these patients might be handled under civilian management. He was an officer who was discharged after 9 days of hospitalization since his duties did not necessarily involve strenuous use of the arm. Incidentally in civilian practice many of these patients would be treated no doubt, in the home without any hospitalization.

Both groups were treated in an army hospital, and, therefore the period of hospitalization includes the period of convalescence. A comparison of the periods of hospitalization in both groups, therefore, should be an accurate gauge of the method of treatment (Table I). In group 1 (conventional treatment group) in class A, the period of hospitalization varied from 37 to 198 days, with an average of 93 days. In group 2 (active motion management) the hospitalization in class A ranged from 9 days to 51 days, with an average of 36 days. In group 1 class B the hospitalization varied from 85 days to over 118 days. In the latter instance the patient received even further hospitalization in an army general hospital for an unknown duration and with unknown end-results. The average time in this series was

over 107 days. In group 2 class B the period of hospitalization varied very little and averaged 31 days. The 1 patient in class C had a total hospitalization period of 87 days. These figures indicate a much shorter period of convalescence in general for the second (active motion) method of management.

#### PERIOD OF DEBILITY

However, in contrasting the 2 methods of management, of even more significance than the total period of hospitalization is the period of time required to attain the end-result functionally (Table II). In this respect, in group 1 the end-result functionally was equivalent to the total period of hospitalization as given heretofore. But in group

class A, function was attained in from 17 days to 42 days with the lone exception of 1 hysterical, uncooperative individual who required 49 days. The average time was 30 days. In group 2 class B there was less variation and function was attained in an average time of 48 days. This average also is a distinct improvement over that for patients in the first group.

## FUNCTIONAL RESULTS

An attempt has been made to estimate the end-result in percentage of function. Where no limitation in range of motion was present, or only 5 degrees' limitation by actual measurement, and with normal, painless muscle power, function was listed as 100 per cent. When there was good function but even 10 degrees' limitation of range of motion by measurement, function was estimated at only 95 per cent, although actually no disability was present. Other cases were definitely graded lower because of obvious disabilities being present.

From this standpoint, in group 1, class A, there were 2 patients with 100 per cent function, and 1 patient with about 70 per cent function. In group 2, class A, all 11 patients had 100 per cent functional end-results. In group 1, class B, the 3 patients were functionally rated 80 per cent, 90 per cent, and 50 per cent under the conventional method of management. But in group 2, class B, 5 of the 7 patients attained 100 per cent function, and 2 patients were rated 95 per cent, although no actual disability was present. These last 2 cases were complicated by complete posterior dislocation of the elbow at time of injury and are, therefore, directly comparable to the relatively poor results obtained in similar cases in group 1, class B. The lone patient in group 1, class C, was rated 60 per cent functional end-result.

## CALCIFICATION IN SOFT TISSUES

Some interesting sidelights on particular patients in this series were discovered. Of the 7 in group 1, 5 showed evidences of calcification in the soft tissues about the elbow. One of these had marked calcification apparently in an area of hematoma following the fracture-dislocation of the elbow. Of the 18 in group 2, only 1 showed any tendency to calcification in the soft tissues, and this to a much lesser extent, although this patient was also a fracture-dislocation of the elbow with marked swelling of the joint after injury. This difference was attributed to the improved circulation from the use of continuous hot packs until the soft tissue reaction had subsided.

## DISPLACEMENT OF FRAGMENTS

In the cases in group 1 the follow-up x-ray films showed essentially no change in the position of the capital fragments after reduction, however, in group 2 there were 5 patients whose checkup films showed slight to rather definite further displacement of the small, uncontrollable fragments of the head of the radius, and yet these patients were all progressing in function under the active

motion management to a very satisfactory (95 to 100 per cent) functional end-result. One interesting patient incurred a comminuted fracture of the head of the radius with a longitudinal splitting and impaction of the neck of the radius with moderate displacement of fragments, but under the active motion management attained 100 per cent function in 6 weeks, and checkup films showed, curiously enough, a more normal appearance with less displacement of fragments, only 2 small fragments being visibly displaced as compared with 4 fragments on the original film. These findings are corroborative of the premise presented above, namely, that anatomical reposition of the displaced fragments is not necessary to regain synchronization of the multiple joint surfaces, but rather that early active motion permits these fragments to assume the optimum functional position in relation to the fixed, uninjured articular surfaces.

## FOLLOW-UP

In postulating any conclusions from this series it must be admitted that the follow-up period is inadequate. With less than 1 year's observation of results it is not possible to exclude subsequent development of posttraumatic arthritis in the cases under the active motion regimen. Unfortunately, with the rapid transfer of army personnel at the present time, supplemental information regarding this possibility will probably be unobtainable. However, it is our opinion that this series presents some valuable points for consideration. The following case abstracts exemplify some of the results analyzed.

## ABSTRACTS OF CASE REPORTS

*Group 1*

**CASE 3.** A 30 year old soldier was admitted to the Station Hospital on August 27, 1941, with the history of having sustained a fall the previous day during 2nd Army maneuvers, landing on right hand, with the elbow bent to an angle of 90 degrees and the forearm pronated. A laceration of the right thumb was sutured at a civilian hospital, and the patient was then transported to Camp Robinson. An x-ray picture taken on admission revealed a complete posterior dislocation of the right elbow, and a chip fracture of the head of the radius. The dislocation was reduced under gas-oxygen-ether anesthesia, and the arm was immobilized at a right angle with a plaster splint. The splint was removed at the end of 3 weeks, and motion was resumed. Appreciable limitation of flexion, extension, and rotation persisted despite all efforts of physiotherapy. On October 9, 1941, under intravenous pentothal sodium anesthesia, the right elbow was manipulated, with temporary increase in the range of motion which lasted only a few days. An x-ray film taken on December 1, 1941, revealed a large calcifying hematoma in the soft tissue about the elbow joint. On December 23, 1941, after 118 days of treatment, the patient was transferred to an army general

hospital. At time of transfer he had an estimated 90 per cent function of the right elbow.

**CASE 6.** A 24 year old soldier, as admitted to the Station Hospital on October 26, 1914, with an injured left elbow sustained that day when he fell, landing on the elbow. X-ray examination revealed fracture of the head of the radius, involving the articular surface. Closed reduction and the application of long arm plaster cast was performed the following day. Motion was resumed after 3 weeks, with appreciable limitation of motion persisting. The elbow was manipulated under general anesthesia on January 3, 1915, with some improvement. Continued physiotherapy as unavailing, and the patient, as transferred to an army general hospital on February 3, 1915. After 93 days of hospitalization, with function of 70 per cent, the left elbow X-ray examination revealed some calcification of the soft tissues and mild traumatic arthritis.

### Group

**CASE 4.** An officer, aged 35 years, was admitted to the hospital on June 20, 1914, with history of having fallen the previous day while running an obstacle course, landing on the point of his left elbow. Examination of the left elbow revealed moderate swelling and limitation of all movements, x-ray tenderness over the head of the radius. Stereoscopic x-ray films of the elbow revealed simple, complete, linear fracture through the antero-medial aspect of the head of the radius, involving the articular surface, with slight downward displacement of the smaller fragment. The closed treatment, consisting of immediate active motion, hot packs, and an arm sling as the only source of immobilization, was instituted. Rapid improvement of function followed. The patient, whose duties did not require strenuous use of his arm, was discharged on the 9th hospital day.

His instructions to continue wearing the sling and to be followed as an outpatient. The function of the elbow at the time of discharge was as follows: flexion to 40 degrees, extension to 45 degrees, 110° per cent supination and pronation. There was no pain, swelling, or instability. Follow-up of the patient revealed complete return of function at 3 days. X-ray film taken 4 weeks post trauma showed an indistinct fracture line and the same deformity as noted on the initial films. No excess callus as demonstrable.

**CASE 5.** A soldier, aged 30 years, was admitted to the hospital on June 3, 1914, with an injured left elbow sustained that day when he fell backward as he swung off horizontal bar landing on his left elbow. Examination of the elbow revealed appreciable pain and swelling. The great limitation of motion and point-tenderness over the head of the radius. X-ray examination revealed simple, complete, comminuted fracture through the antero-medial aspect of the head of the radius, involving the articular surface and extending down into the shaft of the bone, splitting it for distance of 3 centimeters. The immediate active motion treatment as instituted. In 4 days flexion and extension were about normal, but there was slight limitation of both supination and pronation with pain on the extremes of these motions. Muscle power was normal, and there was no instability. The full range of supination and pronation was gradually obtained, and in 6 weeks there was full return of function without any pain, edema, or instability. X-ray films showed the same position as on the initial films. The fracture line was less distinct, and no excess callus formation was noted.

**CASE 2.** A 3 year old soldier was admitted to the hospital on July 27, 1914, with an injured left elbow sustained the previous day when he fell, his running an obstacle course, and landed on his left elbow. Examination revealed pain, swelling, limitation of motion, and point of tenderness

over the head of the radius. Stereoscopic x-ray films revealed an incomplete fracture through the lateral rim of the head of the radius, involving the articular surface. The slight distal displacement of the smaller fragment. The active motion treatment was instituted with rapid return of function. Within week, extension, pronation, and supination were normal, and flexion was slightly limited to an angle of 40 degrees. There was complete return of function at the end of the 2d week when the patient was discharged from the hospital. At this time an x-ray picture showed the fracture line to be less distinct. No callus or change in position as noted.

**CASE 3.** A 27 year old soldier was admitted to the hospital on July 28, 1914, with severely injured left elbow sustained that day when the patient fell while running an obstacle course, landing on his left palm. At the elbow bent to right angle and the forearm in midpronation. Clinical examination revealed an obvious complete posterior dislocation of the radius and ulna on the forearm. This was corroborated by x-ray examination. The initial films failed to reveal any fractures of the radial head. There was marked swelling and ecchymosis about the elbow. The dislocation was reduced by manual traction under pre-tibial sodium anesthesia. The arm was immobilized with only sharp hot packs over applied, and active motion instituted. Stereoscopic views of the elbow taken 4 days later revealed 3 small chip fractures off the lateral aspect of the head of the radius. 13 weeks there was moderate return of function with flexion to 60 degree angle and extension to 60 degrees. Pronation and supination were 85 per cent and 90 per cent, respectively. Muscle power was good. Evidence of considerable ecchymosis persisted. At the end of 3 weeks, flexion was 45 degrees, extension was 40 degrees, and both pronation and supination are 100 per cent. There was no pain or instability. There was no further return of flexion, and the patient was discharged at the end of 7 weeks. X-ray examination at the time of discharge revealed no change in the appearance of the fractured head of the radius. No callus was noted, but there was some calcification in the soft tissues lateral and inferior to the lateral and medial epicondyles.

### SUMMARY AND CONCLUSIONS

1. A survey of the literature reveals that the treatment of fractures of the head of the radius is a controversial matter and with generally not too satisfactory results.

2. A series of 25 cases of fracture of head of the radius is presented.

3. One group of 7 cases was treated under conventional management with generally unsatisfactory results.

4. A second group of 8 cases was treated without fixation, with local heat, and early active motion. The results, as measured by comparable periods of hospitalization, absence of complications, and estimated percentage of function (95 to 100 per cent) were a distinct improvement.

5. The classification used in this discussion limits conclusions to be drawn only as regards linear transverse or comminuted fractures of the head and neck of the radius with no displacement or with only mild displacement of the fragments.

6 Inadequate period of follow-up precludes the elimination of posttraumatic arthritis as a possible late complication under this management, although no patients to date have manifested any symptoms

7 A rationale for the active motion and local heat management is advanced chiefly on the following basis

a The elbow is anatomically a multiple joint with synchronization of joint surfaces being essential to function

b The fractured fragments of the head of the radius are characteristically small and uncontrollable

c Early active motion permits these fragments to be moved across the fixed uninjured articular surfaces of the elbow joint to attain the position where maximum function is possible

d The use of local heat in the form of hot packs permits early elimination of soft tissue reaction and lessens the tendency, frequently seen under conventional management, of calcification of soft tissues about the injured joint

## REFERENCES

- 1 BOHRER, J V *Ann Surg*, 1932, 97 204-208
- 2 COHN, ISADORE *Am J Surg*, 1942, 55 210-227
- 3 COLP, RALPH *Internat Clin*, 1930, 2 208-212
- 4 CUBBINS, W R, CALLAHAN, J J, SCUDERI, C S *Am J Surg*, 1938, 42 627
- 5 ELIASON, E L, and JOHNSON, J In Christopher's A Textbook of Surgery P 566 Philadelphia and London W B Saunders Co, 1936
- 6 ELIASON, E L, and NORTH, J P *Am J Surg*, 1939, 44 80-99
- 7 HEIN, B J *Indus M*, 1937, 6 529-532
- 8 KEY, J A J *Am M Ass*, 1931, 96 101-104
- 9 KEY, J A, and CONWELL, H E The Management of Fractures, Dislocations, and Sprains 2d ed, Chapt 18 St Louis C V Mosby Co, 1937
- 10 KING, B B J *Bone Surg*, 1939, 21 839-857
- 11 MAGNUSON, P B Fractures, 2d ed Philadelphia, Montreal, London J B Lippincott Co, 1936
- 12 NEUWIRTH, A A J *Am M Ass*, 1942, 118 971
- 13 SCHWARTZ, R P, and YOUNG, F *Surg, Gyn Obst*, 1933, 57 528-537
- 14 THORNDIKE, A, JR, and DIMMLER, C L *N England M J*, 1941, 225 475-480
- 15 WILSON, PHILIP D Management of Fractures and Dislocations Chapter VI Philadelphia J B Lippincott Co, 1938
- 16 *Idem Surg Gyn Obst*, 1933, 56 335



# THE RATE AND NATURE OF EPITHELIZATION IN WOUNDS WITH LOSS OF SUBSTANCE

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**I**N the previous attempts made to calculate the rate of epithelization, microscopic cross sections were cut from healing wounds with loss of substance and the length of extension of new epithelium from the old was calculated for the number of days of existence of the wound. This method was used by Akatwa in 1919, in Loeb's laboratory and has recently been employed again in the study of wounds by Dann, Glucksmann and Tanaley and by Olson, Skider Clark and Mac Donald. In the last 2 studies no allowances were made for the presence of a latent period when epithelization does not occur. In Akatwa's work, more attention was given to the number of mitotic figures which were present than to the rate of epithelization.

The nearest approach to a satisfactory method of measuring the rate of epithelization without recourse to biopsy, was described by Carrel and Hartmann. They measured and plotted the change in the size of the original outline of the wound and in the size of the unepithelized area during healing. By subtracting the size of the unepithelized area from the size of the wound as contraction occurred, the amount of epithelization could have been determined. Actually however, these investigators never did calculate the rate of epithelization.

Previous methods had the objections that (1) the size of the wound could be decreased by contraction and (2) there was no satisfactory measure of the progress of epithelization. This paper presents a method free from these objections.

## METHOD

In this investigation, color photography was used to record the progress of epithelization.

In order to eliminate contracture from influencing the results, the outward growth of epithelium from an island of skin was measured. Any change in the size of this island caused by contraction could be readily observed. Further the wounds were placed on the ears of rabbits where contraction is minimal because of the peculiar anatomy. Here the skin rests only on a small amount of connective tissue surmounting cartilage.

A defect approximately 2 centimeters square was cut in the skin on the outside of the rabbit's ear leaving uninjured the blood supply in the base of the defect and the small square island of skin of approximately 2 x 3 square millimeters at its center. To prevent wrinkling and deformation,

rubber form was affixed within the ear by means of adhesive plaster. The desired dressing was placed over the wound and a hood of muslin or oiled skin, tailored to fit and opening by means of snaps, was then sutured to the base of the ear. These hoods were sewed together with 2 or 3 stitches on their inner margins causing them to hang like a cape over the back of the animal instead of weighing each ear down separately. With the protection afforded by these hoods, bandages were rarely lost, and either wet dry or ointment dressings could be employed within them.

To photograph the island, the rabbit was placed in a box which held its head securely in an upright position. A small movable table was placed on top of this box behind the ears of the animal and the ear fastened to it in a relatively flat position by inserting pins through the rubber form. A precision photographic enlarger equipped with 1:5 lens and a 35 millimeter camera and slide viewing back was used to make the Kodachromes (Fig. 1).

A cleared area in the ground glass of the slide viewing back allowed accurate focusing by means of magnifying glass. Two small spotlights were thrown on the wound from opposite sides at 45 degree angles, thereby reducing the number of highlights. This illumination was controlled by a high-low switch to minimize drying while correct focus was being obtained. The wound was also kept moist with saline solution.

In order to obtain the same relative magnification for each photograph, standard bellow length was employed. Focus was obtained by raising and lowering the object under the camera by means of an adjustable table. A sterile steel rod, measuring 5.0 millimeters in length was photographed on each wound. The degree of enlargement of this rod was checked on the viewing glass before the picture was taken. A standard enlargement of 11

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\*Designed by Miss Dorsey Mapes, nurse in charge of the animal operating room.

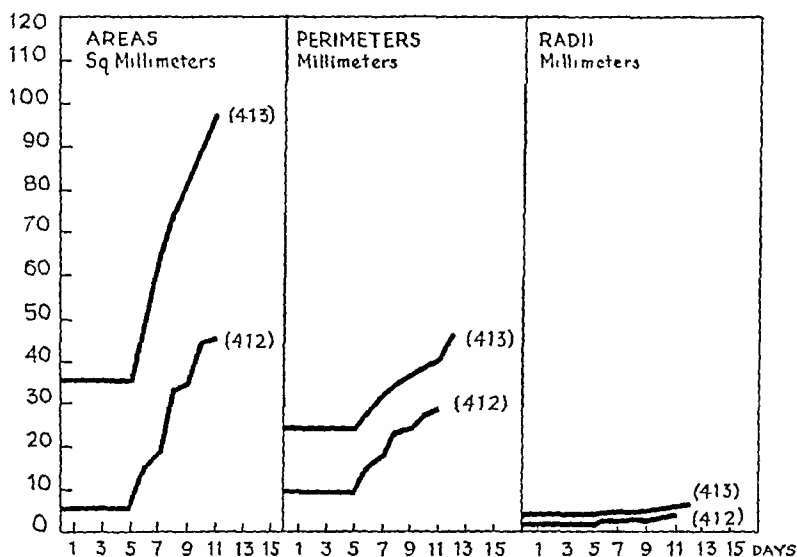


Chart 1 Comparison of increase of large (413) and small (412) islands of skin

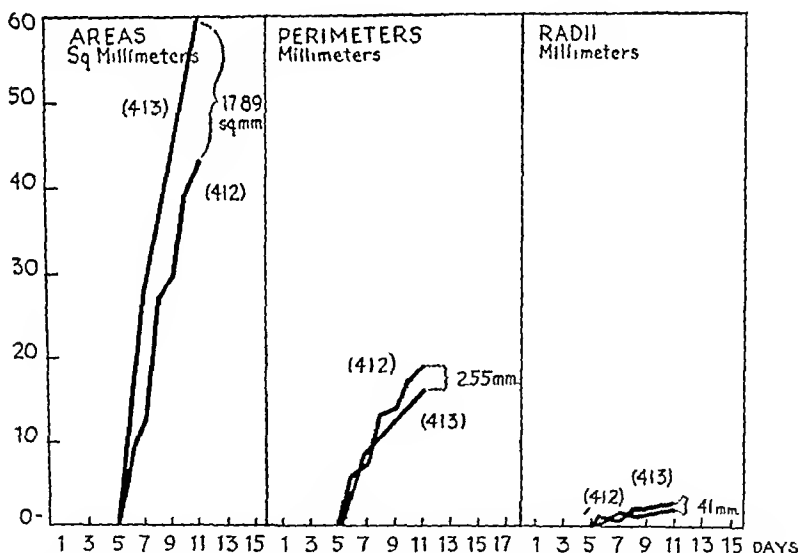


Chart 2 Comparison of growth of large (413) and small (412) islands of skin plotted by daily increments

was employed to measure changes in size of the island during healing after the film was developed

Growth of the epithelizing island was measured by projecting the kodachrome from the enlarger onto a sheet of bond paper. The steel rod was magnified to 50 millimeters, which is ten times its actual size. The outline of the island was then traced, cut out, and weighed. The area of this

tracing was calculated by the gravimetric method of Douglas (4)—the weight of the tracing being divided by the weight of a known unit of area of the paper. Allowance was made for the degree of enlargement.

Microscopic sections were cut from these islands at various intervals to study the progress of epithelization.

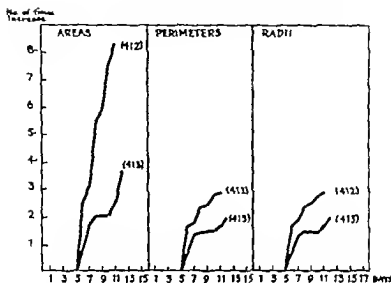


Chart 2. Comparison of large (A) and small (B) islands of skin plotted as number of times increase over original.

#### THE LATENT PERIOD

There was a latent period of 4 or 5 days duration before epithelization started. Extremes of 3 to 6 days were observed without evidence of infection to account for the longer periods. As soon as epithelization began, the edges of the square flattened and bleeded with the surrounding granulations. The sharp cut edge disappeared. The center island became round, and further growth enlarged the circle.

Repeated daily dressings prolonged the onset of epithelization. A latent period of 6 days was obtained, for example, when dressing was changed every day beginning on the 1st day while if this same type of dressing was left undisturbed, epithelization was either just beginning when it was removed on the 4th day or the process started on the following day.

#### MEASURING THE RATE OF EPITHELIZATION

From the start of the experiments it was obvious that some decision had to be reached as to the proper method of expressing the rate of epithelization. Should area be employed or the number of times the area increased in size or the change in the length of perimeter or the rate of linear extension? To determine the proper measurement to employ, epithelization was compared about a small and large island of skin by three different measurements: increase in the area, increase in the perimeter and increase in the length of the radius. Daily increments of these increases were

also compared as well as the number of times each one increased over the original measurement. Chart 1 shows that about a large and small island only the measurements increased at the same rate—the perimeters and the radii. On the contrary the areas of each island increased at different rates varying with the size of the original island. The chart of the increments (Chart 2) beginning as they do at zero, exaggerates both the similarity in the rate of increase of the perimeters and radii and the difference in the rate of increase of areas. Chart 3 shows the number of times these measurements increased over the original ones. This method fails to give linear curves, and cannot be used because differences in the original measurements always distort the answers. Epithelization, therefore, must be expressed in terms of linear extension i.e. change in the length of the radius or change in the length of the perimeter. Inasmuch as change in the length of perimeter is too difficult to grasp, extension of the radius will be employed.

After the latent period, epithelium did not extend at constant rate each day. Chart 4 shows the daily growth from several islands dressed with different substances. On some days there was marked extension of epithelium while on others only small or intermediate amounts of extension

Although the original area, perimeter, the radius of each of these points is used for the comparison. The radius of each point is less than the half of the square of its area. The perimeter is constant and the difference small. Dr. Henry Thomas has checked the mathematics accuracy of these statements.

MILLIMETERS

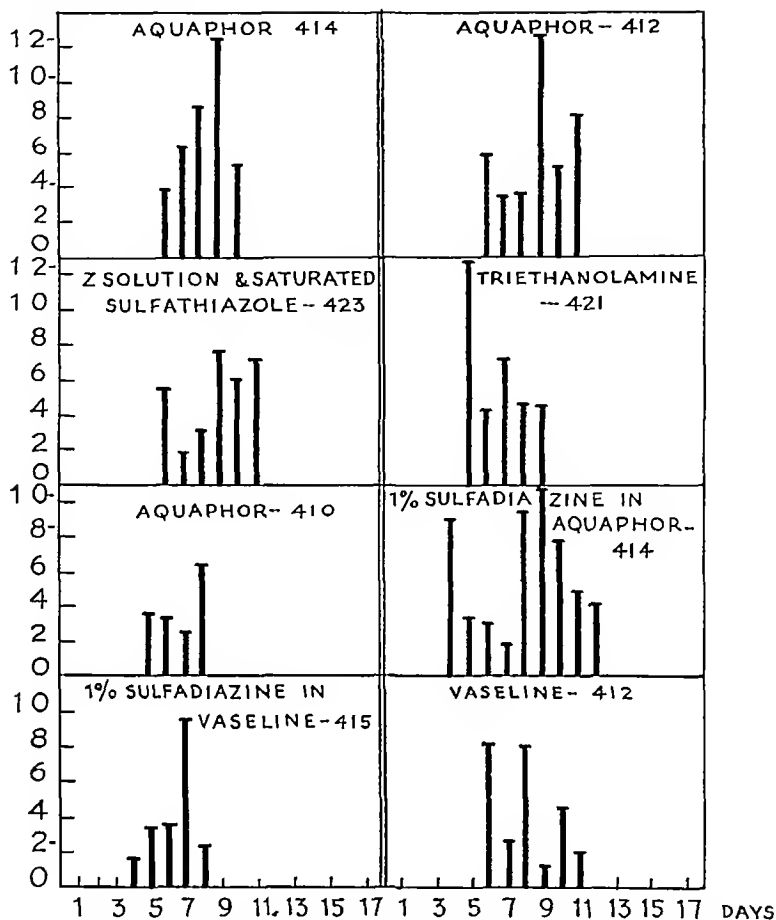


Chart 4 Shows the daily growth of epithelium from center islands dressed with various therapeutic substances. Note that in the three islands dressed with aquaphor there is no rhythm to this extension. The wound dressed with 1 per cent sulfadiazine in aquaphor illustrates a good rate of epithelization.

ere recorded even when the same substances were employed. No rhythm could be found for these variations except that 2 days of marked extension seldom occurred together, and that when a good rate of epithelization was obtained throughout a period of healing by the employment of a beneficial therapeutic substance, there were fewer days with a poor amount of extension. On the other hand, even when a poor rate of epithelization was obtained there were still days of explosive extension in a general pattern of small daily increases. Infection not only stopped the rate of extension, but in some instances actually caused a regression of growth obtained. When infection subsided, subsequent extension was also explosive.

The average rate of epithelization was found to be 0.5 millimeter per day.

#### GROSS CHANGES DURING EPITHELIZATION

A suitable granulating base was needed to allow epithelization to begin. This base had to be free of exudate, red, not too uneven, and neither elevated above nor depressed below the surrounding skin margins.

The advancing margin of new epithelium appeared as a thin bluish white border devoid of normal pigment and hair follicles (Fig 2). To the naked eye this margin seemed regular, although when it was viewed through a magnifying glass the edges were slightly serrated. Irregular-

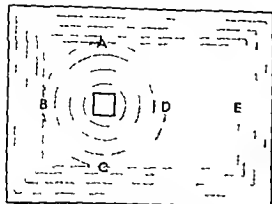


Chart 5. Schematic illustration of geometric patterns in epithelization. The outside heavy black line represents skin edges of the defect. The small square of contiguous black represents the center island. The dotted lines show the extending epithelium. Actually the corners of the epithelium advancing from the edges of the defect should be slightly rounded.

ities were more marked when the surfaces of the granulations were uneven.

The very edge of the advancing margin of epithelium was often not attached to the underlying granulations and could be turned back for a very short distance by means of a cotton swab. A quick pull on this free margin would strip back the new epithelium from the granulations for considerable distance and cause bleeding. Tearing of the free margin occurred when adherent dressings were removed. Immediately behind the margin, the new epithelium was a dull white and was thicker.

As regenerating epithelium also advanced inward from the periphery of the defect the corners tended to round and rarely an island of epithelization would suddenly appear in the midst of the granulations. This unexpected growth apparently originated from undestroyed epithelial cells about a hair follicle or skin gland. The average linear extension from the edges of the defect was identical with that from the center island. No consistent predilection of one edge to extend more rapidly was observed in spite of the fact that the one nearer the base of the ear theoretically should have had a better blood supply.

#### MICROSCOPIC CHANGES DURING EPITHELIZATION

Epithelization was characterized by four microscopic changes: (1) hypertrophy of the uninjured epithelial cells at the wound edges, (2) migration of uninjured cells outward over a suitable granulating base, (3) mitotic division, and (4) retraction of the extended portion.

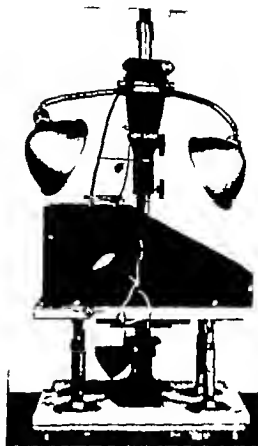


Fig. 4. Apparatus used for taking photographs.

Hypertrophy of the old epithelium at the wound edges extended backward for a distance of 3 or 4 millimeters (Fig. 3). It began to appear about 24 hours after wounding and even epithelium about adjacent hair follicles sometimes became involved. Both the nuclei and cytoplasm of the cells in all layers of skin increased in size, including those below the keratin layer which had already lost their nuclei. Mitotic figures were rare. The cells immediately beneath the pigment and the germinal layer which ordinarily are parallel to the surface of the skin became vertical to it. The cells in the germinal layer appeared crowded together but still contained only an occasional mitotic figure. This hypertrophy resulted in crowding of cells at the edge of the wound about the 4th day after wounding.

Following this hypertrophy cells from the germinal layer extended laterally over the defect. These flattened into a single layer (Figs. 4 and 5).



Fig. 2. A 13 day wound in the ear of the rabbit magnified 2.1 times. The rod measures 0.5 centimeter. The outside black line denotes the original area of the wound. There has been no contraction. Inside this line is a rim of new epithelium ( $1\frac{1}{2}$  to 2 cm). The circle in the center was originally a square of epithelium (lying under the measuring rod) which has grown out into this shape. Between the circle and the rim are granulations appearing somewhat darker in color. The new growth of epithelium first appeared on the 6th day of healing. The rate of epithelization can be calculated from this photograph. The tip of the ear is toward the left.

The length of the extension from the stratified epithelium was considerable and beneath this extension fibroblasts began to appear parallel to the



Fig. 3. Skin wound in rat's tail—3 days old. Epithelium is just beginning to advance. The defect is on the right. The hypertrophied and thickened old epithelium is in the center. One of the hair follicles is involved.



Fig. 4. The defect is on the left. The single layer of cells advancing from the germinal layer can be seen in the middle of the photograph. It can be seen extending for a considerable distance over the granulations by following the germinal layer outward from the stratified thicker portion.



Fig. 5. High power of the extending cells, present in Fig. 4, showing their relation ship to the surface of the granulations and the accumulations of leucocytes beneath them. Note the absence of mitotic figures.



Fig. 6. Newly reestratified epithelium, showing the amount of keratin on its surface and the character of the cells above the germinal layer. The long axis of these cells are still vertical to the surface. On the right, pigmentation is beginning to reappear. The granulations beneath the epithelium consist largely of fibroblasts and capillaries. The reticulo fibrils are still small and are arranged in many directions.

surface and leucocytes and mononuclear cells became fewer in this zone than farther out in the granulations. Sometimes this zone of extension could be observed grossly as a clear red rim about an island.

Mitotic figures first appeared in the old uninjured epithelium at the edge of the wound. They only appeared in the cells which had already moved out over the granulations after 9 days when thickening took place in more than one layer. This

thickening occurred from the old epithelium outward decreasing in amount to that point where the cells extended in a single row. If this point were sectioned just before another ameboid extension took place, it would appear as a growing point of extending epithelium. In fact this point frequently appeared as a growing point both when epithelization was slow and when it was rapid.

Immediately behind this point, the cells not only arranged themselves in more than one layer, but those in the upper ones again turned with their axes parallel to the surface, their nuclei were lost most superficially, and keratin began to appear on the surface (Fig. 6). The reformed keratin was not as thick as over normal epithelium. After a week, pigmentation began to appear in the cells of the superficial layers. The resulting new epithelial scar was slightly thicker than the old epithelium and its rete pegs did not extend as deeply. There were no hair follicles or sebaceous glands below.

#### GEOMETRIC PATTERNS AND EPITHELIZATION

Epithelization advanced radially outward from the skin island and radially inward from the skin edges until the defect was resurfaced. When contact occurred between the advancing margins at points *A*, *B*, and *C* in Chart 5, lateral extension stopped and restratification took place in the adjacent areas. At the same time, however, lateral extension continued between points *D* and *E* and in the triangles bounded on the inside by *AB* and *BC*. Contact of epithelial cells with epithelial cells stopped lateral extension, therefore, but on the other hand, lateral extension continued without contact.

Tropism was not found to be responsible for a more rapid rate of epithelization when two edges approached each other. In Chart 5, for example, the angles of the triangle closed more rapidly than the area between *D* and *E*, and tropism is the usual explanation given for the rapid closure under these circumstances. The true explanation is much simpler. These areas are small and with epithelium advancing from all margins at the same average rate, naturally the rate of closure was more rapid than over the larger defect.

In these experiments, epithelization was observed for only 2 weeks and consequently the slowing and arrest of the process which follows differentiation of the granulating base was not observed. During these 14 days, however, when the granulations were still fresh, the passage of time did not affect the rate of epithelization. The rate,

for example, was no more rapid when epithelization began than at the end of this time. Instead the variations were daily, and local conditions in the wound largely determined the amount of extension. Lastly no evidence was obtained that a greater rate of epithelization exists when a defect is large than when it is small.

Of course everything which has been said about epithelization in this paper is concerned with the process when there is loss of substance and not with epithelization occurring from an intact basement membrane.

#### SUMMARY AND CONCLUSIONS

- 1 Epithelization begins after a latent period of 3 to 6 days
- 2 Frequent dressings prolong the length of the latent period by tearing away the advancing cells
- 3 The rate of epithelization should be expressed either in terms of change in perimeter or of lateral extension from any one edge
- 4 The average rate of epithelization over recently formed granulations is 0.5 millimeter daily
- 5 The rate of epithelization is not influenced by the size of the defect nor is there a greater rate immediately after the start than there is 10 days later
- 6 Instead the daily amount of extension of epithelium is influenced by local conditions in the wound. Bursts occur in the amount of extension without any particular rhythm
- 7 Infection stops epithelization entirely
- 8 A poor rate of epithelization is characterized by very small amounts of daily extension but still occasional spurts occur
- 9 Microscopically epithelization is characterized by hypertrophy of uninjured epithelial cells at the edges of the wound, migration of uninjured cells outward over a suitable granulating base, mitotic division, and restratification of the extended portion. These processes are described
- 10 The arrest of lateral extension of epithelium is discussed as well as the relationship of geometrical patterns to epithelization
- 11 Tropism was not observed

#### REFERENCES

- 1 AKAIWA, HACHIRO. *J. Med. Res.*, 1919, 10, 371-413.
- 2 CARREL, A., and HARTMANN, A. *J. Exp. Med.*, 1916, 24, 429.
- 3 DANN, L., GLUCKSMANN, A., and TANSLEY, K. *Lancet*, 1942, 242, 95-98.
- 4 DOUGLAS, B. *Ann. Surg.*, 1921, 73, 673.
- 5 OLSON, M., SLIDER, E., CLARK, W. G., MACDONALD, R. *Exp. Biol. & Med.*, 1942, 49, 396-399.



# CONSTRUCTION OF AN ARTIFICIAL VAGINA

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FROM the numerous methods of construction of the vagina which have been introduced within recent years, it is obvious that the ideal procedure has not been found. The disadvantages of the earlier methods, notably those of Bald in and Schubert whereby a segment of the intestine was transplanted into the artificial vaginal cavity were the magnitude of the operation, the serious risk of infection and the instability of the intestinal tissue lining. The newer techniques are relatively safe yet they possess other features which less than much to be desired.

In general the procedures in current use for construction of an artificial vagina are of two types: (1) those wherein some form of skin graft is utilized, and (2) those wherein some type of mold is inserted into the cavity epithelialization of the walls being allowed to take place spontaneously. The majority of the first type have been evolved from Graves' method of elevating two skin flaps from the labia and two from the thigh, and attaching them together and to the top of the opening created between the bladder and rectum. Multiple flaps of this type however are subject to necrosis at their distal ends, which in turn may lead to infection and contracture of the vaginal

vault. The formation of a lining from a tubular skin graft from the inner aspect of the thigh, as advocated by Frank and Geist, is a multiple stage operation, necessitating prolonged hospitalization of the patient moreover. In the event the flaps are successful the lining is bulky and contains hair follicles, and because of the presence of all the skin glands, an undesirable secretion is associated. These methods likewise involve mutilation of the vulva or of the skin of the thigh, which is not a inconsiderable objection to the patient. Multiple small Thiersch grafts, employed by a number of authors, are simple of application, yet are inadequate to insure a stable, durable vaginal lining.

Operations of the second type, wherein the walls of the cavity are kept open by a mold and allowed to epithelialize spontaneously are based upon the theory that the lining thus formed is created from embryonic rests and is therefore normal vaginal mucosa. Wharton who originated this method, has reported successful results in several cases. Such a lining nevertheless, must inevitably contain more or less fibrous tissue and as a consequence, lack elasticity and tend to contracture. In addition, the slow process of complete healing necessitates the prolonged use of some type of obturator. Word, in an effort to facilitate epithelialization, has applied pinch grafts to the vaginal mold before its insertion into the cavity. This method is, in the author's opinion, preferable to the use of no grafts at all, though it might be expected that the intervening raw area could be covered largely by scar tissue as is true when pinch grafts are applied to raw areas elsewhere over the body. Frank (4) has recently suggested a nonoperative technique wherein the cavity is created gradually by successive packings which are each being inserted deeper than the previous one. This procedure possesses the same disadvantage as others wherein no lining is introduced, namely the likelihood of scar tissue formation and the danger of contracture upon removal of the packing. Further, one can seldom count on the intelligent and prolonged co-operation of the patient essential to the carrying out of the procedure.

The most desirable operation is obviously one which is simple of execution and in which is the smallest risk, yet gives the patient a vaginal lining which is both pliable and stable. It would seem impossible to obtain such a lining without the use



Fig. 1. The first mold made of urethane frame covered with rubber sponge to which skin graft is attached is worn for 10 days. The second mold, b, is made of acrolite, a hard, light-weight substance which causes no tissue reaction and permits cleansing of the vaginal cavity without removal. The third mold, c, is a rubber sponge covered with a condom, which is worn during the contracture period to maintain the original size of the vagina.



Fig 2



Fig 3



Fig 4

Fig 2 Case 1 Small vaginal indentation 1 centimeter in depth External genitalia normal

Fig 3 Roentgenogram showing a round vaginal obturator 1 5 inches in diameter inserted into the vagina to a depth of 6 inches 1 year after operation

Fig 4 Case 1 Medium size vaginal speculum inserted into the artificial vagina, showing completely epithelized wall The mucosa is glistening, in contrast to the skin of the thigh

of some type of skin graft large enough to cover the walls of the cavity completely Mucosal tissue would, of course, be preferable, since a sufficient amount is not available, however, one must resort to some other type Occasionally, a blind fistulous tract lined with normal vaginal mucosa is present, even so, the stability of such a lining would be questionable The intermediate skin graft appears to offer the most logical solution to the problem, in that it minimizes the risk of contracture and provides a durable, elastic surface, at the same time necessitating a relatively short period of postoperative care With this in mind, the author has employed a technique embodying the application of intermediate skin grafts of proper dimensions to form a complete lining of the cavity, which is in principle that of the Esser inlay graft Counseller (2) reports successful results by completely lining the vaginal cavity with a free skin graft applied over a hard vulcanite mold, as recommended by McIndoe and Banister After the mold is inserted, the vaginal orifice is closed by approximating the labia minora except for a very small opening just below the urethra for drainage This mold is left in for 6 months, after which the patient wears a glass mold for several months longer He states that

these patients do have discomfort from the mold the first month, but are not bothered thereafter

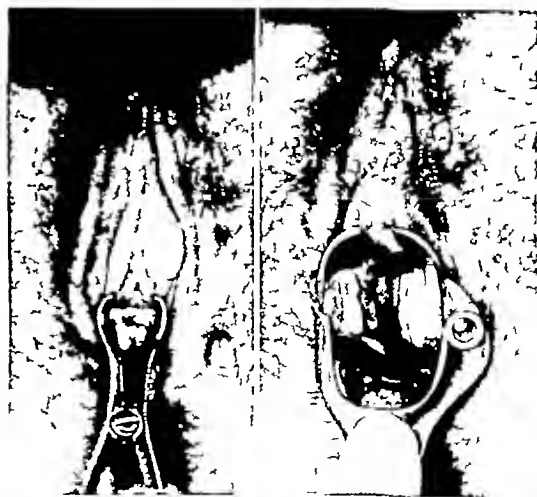


Fig 5, left Case 2 Small vaginal pouch 1 5 centimeters in depth and 0 5 centimeter in diameter demonstrated by means of a nasal speculum Normal external genitalia

Fig 6 Case 2 Medium size vaginal speculum inserted into artificial vagina, showing cavity normal in size and completely epithelized

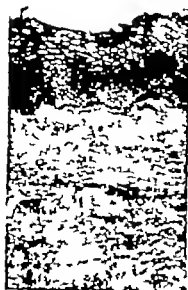


Fig. 7



Fig. 8

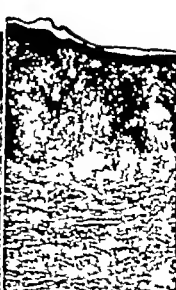


Fig. 9

Fig. 7. Longitudinal section taken of the anterior and middle third of the posterior wall of a normal vagina in girl 8 years of age for comparative study with skin graft lining of the constructed vagina. Note the absence of any stratum corneum or stratum granulosum. No sweat or sebaceous glands. No hair follicles. Basal cells are columnar in type. All the cells above are of the stratified squamous variety. As they near the surface they increase in size and become vacuolated and more clear. This epithelium normally varies in thickness from 50 to 200 microns.

Fig. 8. Section from artificial vagina 1 month after operation. It has the characteristics of skin except for the absence of sweat or sebaceous glands and hair follicles. There is a well developed and adherent cornified layer. The stratum granulosum varies in thickness from 3 to 5

cell layers. The papillae are few and shallow. Basal cells are simple, columnar in type, and contain many mitotic figures. Cells above are polyhedral in shape, and as they approach the surface become more flattened.

Fig. 9. Section from artificial vagina 1 year after operation. The stratum corneum is much thinner than in the 3 month specimen and appears somewhat atrophic. The stratum granulosum layer is quite thin and rarely more than one cell layer in thickness and is occasionally absent, suggesting a decrease in its production of the cells of the corneum. There is an increased thickness of the stratum malpighii, as compared to the 3 month specimen. The papillae are quite numerous and large. The basal cells are columnar in type, but contain comparatively few mitotic figures. Cells above are polyhedral in shape. No sweat or sebaceous glands or hair follicles noted.

Owens has recently reported a case in which he obtained excellent results by completely lining the cavity with one-half thickness skin graft using a vulcanite form held in place by rubber tubes attached to an abdominal binder.

Two cases are here presented in which 3 different types of vaginal molds were used. It is believed that they have definite advantage over other vaginal molds used for this purpose. The first mold is inserted at operation, the second after approximately 10 days, and the third a week or 10 days later.

The first mold consists of a chromium plated, coarse mesh wire frame 4 inches in length and 1 inch in diameter covered by a rubber sponge  $\frac{3}{8}$  inch in thickness. A sponge is selected in which the holes are large and radiate toward the center as the spokes of a wheel, to facilitate drainage into the cavity should this be desirable. A groove

corresponding to the size of the urethra is cut along the upper surface of the sponge to prevent pressure necrosis and fistulization of the urethra (Fig. 8).

This mold has several advantages over those previously used namely (1) it is lighter in weight and therefore more comfortable for the patient (2) being covered with a rubber sponge, the mold permits an even pressure over the entire surface of the graft (3) there is less likelihood of movement of the graft with motion of the patient's body (4) drainage of any area of the cavity through the mold is possible (5) as the opening in the mold extends throughout its length, one can check the progress of the wound at any time and (6) irrigation, if necessary, can be carried out without disturbing the mold or the patient.

The second mold is made of acroclite, hard, light weight material which produces minimum

tissue reaction This mold is similar in shape and size to the first, being 1 5 inches in diameter and 4 5 inches long, though only  $\frac{3}{8}$  inch thick Multiple perforations are made over its entire surface to permit cleansing of the cavity without removal of the mold A notch is made in the outer rim to prevent interference with urination, and behind this notch the mold is grooved as a precaution against undue pressure on the urethral canal This mold is not needed when one obtains a complete take of the skin graft, however, in the event there might be one or more small raw areas it should be used (Fig 1, b)

The third mold consists of a rubber sponge 1 5 inches in diameter and 5 inches long, covered by a condom This mold can be readily inserted and removed by the patient, is easily cleaned, and is worn without discomfort (Fig 1, c)

#### CASE REPORTS

Mrs D P, an attractive white girl, aged 16 years, was referred for construction of a vagina, July 25, 1940 According to her history, she had never menstruated, although at irregular intervals during the previous 2 years she had experienced a slight low abdominal discomfort simulating menstrual pain She had not had any serious illnesses nor any operations She had married without knowledge of her condition, and after marriage had consulted her family physician because of inability to have intercourse Believing that she had an imperforate hymen, the physician had attempted to correct the condition by a simple incision, it was then discovered that she had no vaginal cavity

The patient was well developed, her breasts were of normal contour, and there was no evidence of glandular disturbance No tumefaction was palpable in the abdomen On bimanual examination with the finger in the rectum, a small, mobile uterus could be detected The examination was otherwise negative The external genitalia were normal Just below the urethral orifice was a small indentation approximately 1 centimeter in depth (Fig 2) This was surrounded with scar tissue, probably the result of the incision made 3 weeks before for the supposed imperforate hymen In order to determine whether or not a vaginal fistulous tract was present, lipiodol was injected into the very small shallow pouch under pressure and a roentgenogram was made, no evidence of such a tract was observed

Prior to operation, the intestinal tract was evacuated, that bowel movements might be delayed as long as possible after operation

**Operation** General anesthesia with ethylene gas was used A vertical incision was begun just below the urethral os and continued down to the junction of the labia majora With a catheter in the urethra and a finger in the rectum, an opening between the bladder and rectum was made by blunt dissection, its depth and diameter corresponding to that of the mold to be inserted subsequently, so that its surface would fit smoothly and evenly throughout Only a thin layer of connective tissue intervened between the bladder and rectum, and extreme care was necessary in making the dissection to avoid perforation of the walls of these structures There was no cervix or any tissue present which resembled vaginal mucous membrane

At this point, a condom was slipped over a sponge vaginal mold (Fig 1, c) and inserted into the newly formed cavity to control oozing of blood while the lining was being pre-

pared With a Blair skin graft knife, a split graft of approximately half the thickness of the skin measuring 3 5 inches in width and 7 inches in length was taken from the inner aspect of each thigh Rubber cement was applied to a few small areas on the surface of the sponge covering the wire mesh frame (Fig 1, a), to obviate the necessity of suture of the graft yet insure its maintenance in proper position The graft was then applied smoothly over the mold, its raw surface being placed on the outside With a No 11 Bard Parker knife blade, multiple small openings were made through the graft into the rubber sponge, to permit drainage in the event this should become necessary The mold previously placed into the newly formed cavity to stop the small amount of bleeding, was withdrawn and the graft-covered mold was inserted, the groove in the mold being placed directly beneath the urethra Two tension sutures of No 2 Deknatel were passed through the labia majora to help prevent any movement of the skin covered vaginal mold A retention catheter was introduced into the urethra, and remained in place for 10 days, to prevent contamination of the wound with urine after operation

The cavity and mold were inspected daily for drainage On the 5th postoperative day a slight moisture was observed, and saline irrigations of the inside of the vaginal mold were promptly instituted and carried out at frequent intervals Neither the mold nor the patient was disturbed for these irrigations The water remaining inside the mold after irrigation was sucked out with a glass tube attached to a bulb syringe The mold was removed on the 10th postoperative day, and it was found that the graft had taken completely with the exception of one small area approximately 1 5 centimeters in diameter on the right vaginal wall posteriorly The general appearance of the skin graft was typical of the usual split graft to any other part of the body at its first dressing The retention catheter was also withdrawn at this time The specially prepared acrolite mold, which could be removed and replaced as necessary for hygienic purposes, was then introduced into the cavity (Fig 1, b)

The small area on the vaginal wall, where the skin graft failed to take, was watched from day to day for an epithelialization of vaginal mucous membrane or any cellular changes which might suggest regeneration from embryonic vaginal rests, which, according to Mijsherg, Koff, and Vilas, are concerned in the formation of normal vaginal mucosa The area presented all the characteristics of a raw, granulating wound, as was expected Had there been any of the embryonic rests, I feel sure that its surface would have resembled that of normal vaginal mucosa Healing took place as in the ordinary wound, from the periphery inward Two or three weeks later some scar tissue reaction was observed in the area, necessitating digital massage to prevent contracture

The acrolite mold was removed after 1 week, and a solid rubber sponge mold covered with a condom was inserted (Fig 1, c) This mold caused no discomfort and could be easily removed and reinserted by the patient as desired It is worthy of mention that both the acrolite mold and the rubber sponge mold remained *in situ* without the use of a binder or any other support

At the end of 3 or 4 weeks the graft began to exhibit some of the characteristics of normal mucosa, being somewhat pink in color and sufficiently moist to present a naturally glistening surface Tactile sensation was elicited throughout the vaginal wall by the gentle application of a small cotton swab to different points The patient was allowed to have intercourse after 3 months She did not experience an orgasm for several weeks after she began having intercourse The husband reported complete satisfaction from the beginning

The rubber sponge mold was worn continuously for 3 months. The following 3 months the mold was worn about half the time, and for the next 3 to 4 months the mold was inserted at irregular intervals for few hours at a time.

The patient returned May 94 months after construction of the vagina, because of moderately severe low abdominal cramping and an associated dull pain in the breasts, more or less, at monthly intervals. Believing that these symptoms are related to her menstrual dysfunction, she was referred to a gynecologist, who advised exploration. At operation small bicornuate uterus was found. Both ovaries and tubes were normal. A hysterectomy was performed. The ovaries and tubes were not disturbed. Each horn of the uterus measured 9 centimeters in length and 5 centimeters in diameter. At the distal end of the left horn there was small cyst containing a diameter containing thin, clear yellowish fluid. The pathologist reported that the uterus was solid throughout, with no evidence of cavity.

One year after operation round aginal obturator 5 inches in diameter could be inserted easily to depth of 5 inches without any discomfort to the patient (Fig. 3). The lining of the cavity is pink, moist and glistening, closely resembling normal vaginal mucosa (Fig. 4). It is now 27 months since the vaginal construction and the patient is well and happy.

CASE. Miss G. S., white, aged 3 years, was referred by a gynecologist, March 28, 94, for congenital absence of the vagina. She had consulted the gynecologist because of severe low abdominal cramping. She gave history of having had similar attacks since she was 3 years of age. These attacks, as described, are suggestive of menstrual cramping and varied in duration from 1 to 3 days and are from 3 days to several months in occurrence.

On discovering the vaginal anomaly and being unable to palpate any of the pelvic organs rectally the gynecologist explored the patient's abdomen. A bicornuate uterus, each horn of which measured 8 centimeters in length and 1.5 centimeters in diameter was found and removed. Both tubes and ovaries were normal and are left in situ. There is no cervix. The pathologist reported that the two uterine horns are imperfectly fused in the midline, and no cavity could be demonstrated in either.

At the patient's first visit, prior to the hysterectomy the author found rudimentary vagina 5 centimeters in depth and 5 centimeters in diameter (Fig. 5). The external genitalia are normal, and the patient otherwise presented normal feminine physical characteristics. Since there is no occasion for correction of the defect at that time, an operation is not advised.

The patient returned, April 30, 94 stating that she wished to have vagina constructed, as she intended to be married in the near future. The vagina was constructed in the same manner as in the first case presented. In carrying out the dissection for the cavity search as made for aginal tract, though none as found. Two medium thick skin grafts, each approximately 3 by 7 inches in diameter, are taken from the thighs and applied over the exposed covered are with finesse (Fig. 6) and the mold is inserted into the opening. At the conclusion of the operation, retention catheter was placed in the bladder. Both the mold and the catheter are removed on the 10th postoperative day.

Postoperative drainage was negligible, and upon removal of the mold, the lining is found to have adhered throughout. Since the graft had taken completely it is not felt necessary to insert the spongy mold, as was done in the first case. The rubber sponge, covered with concha (Fig. 7) was placed in the cavity immediately. During the remainder of the patient's stay in the hospital, the

mold was removed twice daily for cleansing of the cavity. She was discharged from the hospital 4 days after operation. The rubber sponge mold was worn continuously for 3 months. During the next 3 months it was worn only during the night and for the next few months it was inserted only at varying intervals as check and precaution against any distention in size of the aginal cavity.

The patient, last seen 9 months after operation. The vaginal cavity well maintained its original size and only after very close detailed examination could one distinguish it from normal aginal mucosa membrane (Fig. 8). She stated that sexual intercourse is completely satisfactory and that she had an orgasm with each act.

A comparative study was made of the epithelial lining of the constructed vagina with that of the normal vaginal mucosa membrane. The surface of the grafted lining during the first few weeks has all the characteristics of a split skin graft applied to the external surface of the body. It soon begins to lose the gross appearance of skin and takes on a pink, moist, glistening appearance. During the first 3 or 4 months the surface is rather smooth, after which irregular shallow furrows begin to develop, which closely resemble the rugae of a normal vagina. The secretion of the constructed vagina has never suggested that of the sweat or sebaceous glands of normal skin.

For comparative microscopical study a specimen was taken from the vaginal wall of a healthy nulliparous girl, 18 years of age (Fig. 9). Sections were also taken from the epithelial lining of the constructed vagina at 3 months (Fig. 8) and 1 year after operation (Fig. 9). All specimens are taken at the junction of the anterior and middle one-third of the posterior vaginal wall.

In a normal vagina there is no stratum corneum or stratum granulosum. In the artificial vagina at 3 months, there is a stratum corneum which resembles that of normal skin, being quite smooth and adherent. At 1 year it is much thinner and appears somewhat vestigial.

In the artificial vagina, the stratum granulosum at 3 months appears quite active varying in thickness from 3 to 5 cell layers. At 1 year it is quite thin, rarely more than one cell layer in thickness and occasionally absent, suggesting decrease in its production of the cell of the corneum. The stratum malpighii at 3 months is about one-half to two-thirds the thickness of the 1 year old specimen. The papilli (rete-pegs) 13 months are few and shallow and the car are numerous and larger. The basal cells are simple columnar in type and at 3 months there are many mitotic figures, as compared to only a few 1 year. The cells above the basal layer become polyhedral and as they approach the surface increase in size and become more flattened.

No sweat glands, sebaceous glands, or hair follicles were noted in either specimen. The sub-epithelial layer, which is composed of loose connective tissue, appears the same in all 3 specimens.

The basal cells of the mucous membrane of the normal vagina are columnar in type. All the cells above the basal layer, however, are of the stratified squamous variety. As the cells near the surface they increase in size and become vacuolated and more clear. Maximow and Bloom, in describing the normal vaginal mucous membrane, state that the epithelium is of the stratified squamous variety and has a thickness of 150 to 200 microns. Under normal conditions the superficial cell layers in primates do not show cornification, although they contain granules of keratin. The nuclei usually remain stainable and the cells become loaded with glycogen and fat. In a prolapsed vagina, when the mucous membrane is exposed to air, the superficial cells are cornified as in the epidermis.

Embryologically, the mucous membrane of the vagina and the skin are both of epidermal origin, which may well explain why the mucous membrane when exposed to air over a long period of time, as in a prolapsed vagina, becomes cornified like the epidermis of the skin. This being true, it seems reasonable to assume that the reverse process might take place, when skin placed under the same environment as that of the normal vaginal mucosa would lose the characteristics of normal skin and take on the appearance of the epithelial lining of a normal vagina.

## SUMMARY

A technique is described for complete construction of an artificial vagina in one operation whereby the newly formed cavity is completely lined with a thick split graft ranging from thin to medium.

It is felt that the three types of vaginal molds used play an important part in the success of the operation. The first, which is covered over with a half thickness skin graft and inserted into the newly formed cavity immediately, is made of rubber sponge surrounding a wire framework. This mold is comfortable, very soft, light in weight and affords an even and constant pressure on the skin graft. The second mold, made of acrolite and also light in weight, has multiple perforations permitting vaginal irrigations without removal. The third, consisting of a rubber sponge covered with a condom is worn until all danger of contraction of the skin graft has passed. This mold may be easily removed and reinserted by the patient. All molds described remain in place without the aid of an external brace or support.

Two cases are presented in which excellent results were obtained by this method, both patients reporting satisfactory normal sexual intercourse.

## REFERENCES

1. BALDWIN, J. F. *Ann Surg*, 1904, 40: 398.
2. COUNSELLER, V. S. *S Clin N America*, 1939, 19: 1047.
3. FISSER, J. F. S. *Esser Inlay* Leiden, Holland E. J. Brill, 1940.
4. FRANK, R. T. *Am J Obst*, 1938, 35: 1042.
5. FRANK, R. T., and GEIST, S. H. *Am J Obst*, 1927, 14: 712.
6. GRAVES, WILLIAM P. *Gynecology* 4th ed., p. 794. Philadelphia W. B. Saunders Co., 1928.
7. KOFF, ARTHUR K. *Development of the Vagina in the Human Fetus*, Carnegie Contribution to Embryology 1933, 24: 59.
8. MAXIMOW and BLOOM. *Textbook of Histology* 4th ed. Philadelphia W. B. Saunders Co., 1942.
9. MCINDOE, A. H. and BANISTER, J. B. *J Obst, Gyn Brit. Empire*, 1938, 45: 490.
10. MIJSBERG, W. A. *Zschr ges Anat*, 1924, 74: 684.
11. OWENS, NEAL. *Surgery*, 1942, p. 139.
12. SCHUBERT, G. *Surg Gyn Obst*, 1914, 19: 376.
13. VILAS, E. *Zschr Anat Entw* 1932, 98: 263.
14. WHARTON, LAWRENCE R. *Ann Surg*, 1938, 107: 842.
15. WORD, BUFORD. *South M J*, 1940, 33: 293.

# EDITORIALS

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## SURGERY Gynecology and Obstetrics

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JUNE, 1943

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### THE RELATIONSHIP OF FRACTURES TO SEVERE PAINFUL JOINT LESIONS OF THE LOWER EXTREMITY

WITH the increased knowledge of various types of complications arising from fractures adjacent to joints, a wider realization of the importance of more accurate and complete reduction of all fractures adjacent to joints of the lower extremity has developed. Whether it be a fracture adjacent to the hip the knee or the ankle or of the midtarsal bones, a traumatic arthritis is likely to result which may in time cause a considerable amount of disability.

In the case of the hip joint it is the fractures of the acetabulum which are particularly likely to cause such a complication. Aseptic necrosis may develop after dislocations or fractures of the neck or head and after these have occurred it is very common for a variable degree of traumatic arthritis to develop.

Any fracture about the knee joint and particularly those fractures which have caused

cracks or fissures into the joint, so that the articular surfaces are damaged may lead to traumatic arthritis. Even more important from this standpoint are fractures through the condyle or through the tibial plateaus, which cause the normal alignment of the knee joint to become distorted. Unless the normal alignment is re-established and the axis of rotation is brought back to its normal place constant attrition of the joint surfaces will follow and in time a certain degree of traumatic arthritis will develop which eventually will cause severe painful arthritis to develop in the knee joint.

In fractures about the ankle joint and particularly Pott's fractures and triplanar fractures, similar mechanical factors are concerned. If such fractures are imperfectly reduced they may for a while appear to give little trouble but in time wear and tear on the joint surfaces will result in a painful arthritic joint for which little can be done except arthrodesis. In more severe fractures of this type, with severe damage to the joint surface at the time of injury such a result may develop in spite of accurate reduction of the fracture.

The disabling effects of fractures of the calcaneus are well known. Such effects can arise from traumatic arthritis as well as from malalignment and exostosis about the bone with or without complete reduction. It is rare that a fractured calcaneus heals completely without the causation of any disability.

Fractures of the talus, although not so common as fractures of the calcaneus, are even more of a source of painful disability. Besides the traumatic arthritic changes at times severe aseptic necrosis may develop in a portion of the fractured talus. If it is not recognized

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and the patient is allowed to use the foot, such a condition may lead to severely disabling arthritis. Only with perfect reduction and retention past the time in which such complications develop, can the more troublesome late effects be avoided.

One has only to see a few of these painful joints developing several months to several years after fractures, about the joints of the

lower extremities in particular, to realize the importance of putting forth a greater effort toward restoration of the fragments to as nearly perfect position as possible, and then the need of preventing full weight-bearing until the joint surfaces have had an opportunity to heal completely. If these rules are adhered to, better long range results after such injuries will be obtained.

RALPH K. GHORMLEY



# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

**Clinical Anesthesia.** John S. Lundy has presented the medical profession with nearly 800 pages of very readable, practical, and timely information on a subject in which he is an authority and to which he has made many original contributions. The book represents his extensive personal experience of more than 20 years as head of the section on anesthesia, Mayo Clinic, covering more than 300,000 cases. This experience also spans the events in the development of anesthesia as a recognized medical specialty culminating in the establishment in 1937 of the American Board of Anesthesiology for examination, certification, and control of specialty training in this field.

Of particular interest to the surgeon is the opening chapter in which the choice of anesthetic agents and methods for various operations are carefully discussed in connection with Ingenious charts, which present a check list of approval or disapproval of each anesthetic method in relation to the possible operations in each region of the body and in relation to the patient's physical condition.

Two hundred pages are devoted to the principles and techniques of local, regional, and spinal anesthesia, with numerous illustrative diagrams. Those who have had access to Lebat's *Regional Anesthesia* realize its wealth of detail and illustration on local blocks, but Lundy surpasses former authors in his careful exposition of spinal and sacral block anesthesia. Every surgeon or anesthetist reviewing the two chapters describing Lundy's technique of spinal puncture and principles of the *at glo* dose diffusion method will find emphasis on many valuable and often neglected points. For operations requiring long duration of anesthesia Lundy describes his use of Lemmon's continuous spinal technique.

Over 200 pages are devoted to general anesthesia, including a careful treatment of the methods of inhalation, rectal, and intravenous administration. Most valuable is the author's discussion of the intravenous method with sodium pentothal. Lundy has had the most extensive experience with this agent and method (nearly 5,000 cases reported to 1934) since his introduction of the intermittent injection technique in 1934. Intravenous anesthesia is growing in popularity and use due to its many advantages and holds promise of being quite useful in military and naval surgery. All who intend employing this method should read Lundy's text for information on important precautions in technique, and for the

usual effects and difficulties which may be encountered. Special chapters are included on intratracheal technique and on anesthesia in dentistry, obstetrics and neurosurgery.

Since the military anesthetist, and frequently the civilian as well, is responsible for intravenous fluid therapy including blood, plasma, and serum transfusions, and for apparatus and instruments in the operating room—their care, sterilization, and method of use—Lundy's 6th chapter serves as a valuable manual of instructions to operating room personnel on this subject. The author's oscillatory method of taking blood pressure without stethoscope is simple and convenient. Chapter 23 discusses intravenous therapy and outlines the management of a blood bank and transfusion service. Feeling that those responsible for anesthesia should be skilled in venipuncture, the author describes several techniques for facilitating puncture of difficult veins. Resuscitation procedures are treated in a separate chapter.

The book concludes with several chapters on anesthesia: statistical methods, including an analysis of experiences at the Mayo Clinic from 1924 through 1930, the chemistry of anesthetics and related drugs, historical chronology, conversion tables, method of gas analysis for oxygen tent control, and useful bibliography of books recommended for additional reading supplementing the specific citations ending each chapter. The book contains 266 illustrative figures and 50 charts or tables.

Lundy's emphasis on the clinical problems of anesthesia is exemplified by the frequent introduction of interesting case histories and specific incidents in the author's experiences which serve as colorful illustrative material.

The text is replete with practical points and refinements of technique which have not occurred to the casual reader who may take note and apply them with benefit to both patient and surgeon. That the book summarizes the author's own personal beliefs and experiences is shown by the exclusion from detailed consideration of certain methods, goals and techniques which he has tried but found dangerous, unsatisfactory or unnecessary.

There has long been a need for this modern treatise on American anesthetic methods. It is fortunate to have Lundy's book available as a companion text and reference for the current courses in anesthesia for medical officers of the armed services. *Clinical Anesthesia* is heartily recommended for addition to the current working library of surgeons and physicians anesthetists both at home and abroad.

II CH O BROWN

## REVIEWS OF NEW BOOKS

AS noted in the preface, *Traumatic Surgery of the Jaws*<sup>1</sup> is presented to assist the dentist in his preparation for first aid and emergency treatment of jaw injuries. However, any general surgeon who may be concerned with the treatment of these will find much of interest and value in it, though he will doubtless be inclined to skip some of the elementary treatises on shock, burns, anesthesia, osteogenesis, etc. The appearance of this book is timely, as reports indicate the occurrence of large numbers of facial injuries in the present mechanized warfare.

The book is well written, and the illustrations are excellent. The author concurs with the increasingly prevailing opinion that complicated dental splints are neither necessary nor desirable in the treatment of jaw fractures, and admirably refrains from their description. However, seven methods of interdental wiring are described, not all of which seem to possess intrinsic advantages over the others in any given situation. The necessity for, and evolution of, new methods of, direct skeletal fixation for edentulous fragments are noted.

From the surgeon's point of view, a more inclusive work dealing with the care of all soft tissue and bony injuries about the face and jaws might be preferable. Extensive and serious lacerations, depressed orbital floors, and compound nasal injuries are not infrequently associated with severe jaw injuries, and their care may be so intimate as to be almost inseparable. Minor faults include the statement that "syphilis is an important cause of nonunion," the lack of attention to surgical drainage of infections which may occur around fractures, and the description of treatment of ununited fractures in four sentences. These do not detract greatly from the general utility of the volume and the recommendation of it.

FRANK McDOWELL

THE individual manuals of the series of which *Abdominal and Genito-Urinary Injuries*<sup>2</sup> volume is one are prepared under the auspices of the various subcommittees of the committee on surgery and edited by the committee on information of the National Research Council. The committee on surgery is composed of Drs. Everts A. Graham, chairman, Irvin Abell, Donald C. Balfour, George E. Bennett, Warren H. Cole, Frederick A. Collier, Robert H. Ivy, Herman L. Kretschmer, Charles G. Mixter, Howard C. Nafziger, Alton Ochsner, I. S. Ravdin, and Allen O. Whipple. The committee on information includes Drs. Morris Fishbein, chairman, J. J. Bloomfield, John F. Fulton, Richard M. Hewitt, Ira V. Hiscock, Sanford V. Larkey, and Robert N. Nye.

In this volume the section on "Abdominal Injuries" has been prepared by Ambrose H. Storck and contains 11 chapters dealing with "General Considerations," "Study and Estimation of Status of Patients with Known or Suspected Abdominal Injuries," "General Care of Patient, Including Preoperative Preparation," "Preanesthetic Preparation and Anesthesia," "Operative Procedure," "Wounds of Specific Structures and Organs," "Postoperative Treatment," "Complications, and Results, Mortality and Statistics."

The section on "Genito-Urinary Injuries" was prepared and edited by the subcommittee on urology of the committee on surgery. This subcommittee is composed of Herman L. Kretschmer, chairman, William F. Braasch, Frank Hinman, Homer G. Hamer, Oswald S. Lowsley, and Albert J. Scholl, with contributions by Clark M. Johnson and H. M. Weyrauch.

This volume has admirably succeeded in its purpose in conveying to its readers in the smallest compass the greatest amount of practical surgical counsel dealing especially with war injuries of the abdomen and of the genitourinary tract, the evacuation of wounded, types of missiles, and the mechanism of wound production with and without penetration. Shock and hemorrhage are considered. The diagnosis of abdominal injuries is thoughtfully outlined. The chapter on operative procedure contains much useful and practical information. The illustrations are excellent and informative, and the references at the end of each chapter are pertinent and valuable. The editors of the next edition will no doubt correct the duplication of presentation of some of the genitourinary injuries in the two parts of the volume.

In the opinion of the reviewer this small book is an important contribution to the war effort and that it should prove of value to all medical officers in the armed forces and to their patients.

FREDERICK CHRISTOPHER

THE manual entitled *Ophthalmology and Otolaryngology*<sup>3</sup> prepared under the auspices of the National Research Council fulfills rather well its purpose of giving simply, graphically, and not too technically such fundamental knowledge as may be necessary in the field for men without specialist training. Especially does the first section give a well written, well organized, and understandable coverage of methods of examination and medical and surgical care of eye conditions likely to occur in military practice. Discussions of local anesthesia and the simpler injuries, technique of local anesthesia and the simpler surgery of the lids and orbit are good.

The section on otolaryngology is somewhat uneven and some chapters seem to have been hurriedly written. The selection of material and its emphasis for such a manual must have been difficult but one might question, for instance, why mastoiditis is only casually mentioned while considerable space is given to the rather technical discussion of petrositis and operations for its relief. The chapters on wounds and

<sup>1</sup>TRAUMATIC SURGERY OF THE JAWS INCLUDING FIRST AID TREATMENT. By Kurt H. Thoms, D.M.D. St. Louis: C. V. Mosby Co. 1942.  
<sup>2</sup>ABDOMINAL AND GENITO-URINARY INJURIES. A Military Surgical Manual Prepared under the Auspices of the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Philadelphia and London: W. B. Saunders Co. 1942.

<sup>3</sup>OPHTHALMOLOGY AND OTOLARYNGOLOGY. Prepared and edited by the Subcommittees on Ophthalmology and Otolaryngology of the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Philadelphia and London: W. B. Saunders Co. 1942.



## REVIEWS OF NEW BOOKS

sinuses, and mastoids. An abstract of an article on origin and management of occipitoposterior position in labor, has crept in, which contains no reference whatever to radiology.

The section on therapeutics is divided into 16 chapters. The editor's introductory chapter covers in general the remainder of the section and correlates the main points and conclusions of the abstracted articles which follow. Its organization makes this chapter as easily read as a textbook. Following many of the abstracts the editor discusses the article concurring or differing with the author, enlarging on a point, citing previous references, and adding the benefit of his experience. In the treatment of malignant growths he is not partial to x ray, radium, or surgery at the expense of either of the other two, this attitude makes his viewpoint all the more valuable.

The book is an excellent reference source and should be available to everyone interested in the practice of the specialty. I. I. JENSEN

MANY well known authors have contributed to this symposium monograph. A large part of the book comprises papers which were presented at the annual meeting of the American Human Serum Association held in June, 1941 at Cleveland. In certain cases the results of additional work which was done by the authors between the time of the presentation of the papers and the reading of the proof are introduced. The book contains much interesting and valuable information. It can be read and understood both by the specialist and the individual who may be seeking an answer to problems relative to the use of whole citrated blood, blood plasma, blood serum, and other blood substitutes. The last chapter is a well written summary. It contains such information as "the successful management of shock requires early recognition and effective measures for breaking the vicious circle. These will be directed toward removing the cause toward increasing the blood volume and toward relieving anoxia." The advantages and disadvantages of the four general methods for preservation of plasma and serum are discussed. Hemoglobin serum albumin and serum digest as blood substitutes are considered. A good presentation is made of the storage, transport, and administration of whole blood. The Rh factor and the specific A and B factors are readily understandable by reading this book. The use of frozen blood withdrawn from so called universal donors is discussed. This book is valuable for the general practitioner and specialist alike. It is interesting, informative, and later editions will be looked for.

THE little book of 354 pages *Recent Advances in Obstetrics and Gynecology* by Bourne and Williams does not claim to be a compendium of obstetrics and gynecology. It takes up the important chapters in both fields and discusses the progress which has been made in recent years. The author does not limit himself to the work of the British clinics but work done on the continent and in America is frequently reported. In the obstetrical portion of the book no attempt is made to cover the field of obstetrics but such subjects as disproportion, anemia, version, chemotherapy, analgesia and puerperal sepsis are considered. The chapter on pelvimetry summarizes very well the work which has been done in a number of clinics in the development of pelvimetric methods, including a review of radiological pelvimetry. The management of puerperal sepsis including a consideration of the present status of chemotherapy, is thoughtfully presented.

In the gynecological section, 39 pages are devoted to cancer and a well organized presentation of present day therapy is given. Radiological statistics from a number of well known clinics are given. The comparison of results of extended operation in cancer of the cervix and radiotherapy is dispassionately given, the author's intention being evidently to present the facts to informed readers for their own evaluation. Sufficient information concerning the present day methods of irradiation is given to indicate the techniques which have been tried in the most active clinics.

Sterility and infections of the cervix and vagina both receive attention. The treatment of the latter is sensible considered without introducing any but the more useful methods. A timely caution appears concerning the proper employment of cauterization and coagulation. The chapter on hormones must be commended. The author travels safely through the quicksands of the consideration of the rarer ovarian tumors. While opinions vary concerning certain of the phases of this subject especially as to certain points of histogenesis this chapter is sane and sound.

Radiology as applied to gynecology is summarized and there is a brief consideration of physiotherapy. A few typographical errors appear, for instance the names of Wertheim and Buring are misspelled the former in one place only. On page 20 the use of the word "destroyed" instead of "described" causes an unfortunate distortion of meaning. These faults may easily be corrected in a later edition.

The book may be recommended to physicians preferably to those who already have some knowledge of the fields presented as a concise and accurate review of the progress of recent years. It will be a useful little volume. W. C. DANFORTH

THE UNIVERSITY OF CHICAGO PRESS  
530 N. Dearborn St. Chicago 12, Ill.  
1942

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1942

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

**BLOOD GROUPS AND TRANSFUSION.** By Alexander S. Wiener, A.B., M.D. 3d ed. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1943.

**A TEXT-BOOK OF PATHOLOGY: A INTRODUCTION TO MEDICINE.** By William Boyd, M.D. LL.D., M.R.C.P. Lond. Dipl. Psych., F.R.S.C. 4th ed. Philadelphia: Lea & Febiger, 1943.

**CLINICAL ROENTGENOLOGY OF THE CARDIOVASCULAR SYSTEM.** By Hugo Rosler, M.D., F.A.C.P. 2d ed. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1943.

**TRANSURETHRAL PROSTATECTOMY.** By Rosal M. Noddi, M.D., F.A.C.S. with chapter on the Vascular Supply of the Prostate Gland by Robin H. Flocks, M.D. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1943.

**OUTLINE OF ROENTGEN DIAGNOSIS, AN ORIENT 1904 IN THE BASIC PRINCIPLES OF DIAGNOSIS BY THE ROENTGEN METHOD.** By Leo G. Rigler, B.S., M.B., M.D. 2d ed. Philadelphia, London, Montreal: J.B. Lippincott Co. 1943.

**CLINICAL SIGNIFICANCE OF THE BLOOD IN TUBERCULOSIS.** By Gail Lloyd Muller, M.D. New York: The Commonwealth Fund, 1943.

**A MANUAL OF OTORHINO LARYNGOLOGY AND LARYNGOLOGY.** By Howard Charles Ballenger, M.D., F.A.C.S. 2d ed., rev. ed. Philadelphia: Lea & Febiger, 1943.

**VICTORIES OF ARMY MEDICINE, SCIENTIFIC ACCOMPLISHMENTS OF THE MEDICAL DEPARTMENT OF THE UNITED STATES ARMY.** By Edgar Erskine Hanna. Philadelphia, London, Montreal: J.B. Lippincott Co. 1943.

**STRUCTURE OF DUCTS OF THE SALIVARY GLANDS.** By Richard L. Saiton, M.D. and Richard L. Saiton, Jr., M.D. St. Louis: The C.V. Mosby Co. 1943.

**ADD TO SURGICAL ANATOMY.** By J.S. Baxter, M.B., M.Sc., F.R.C.S.L. 2d ed. Baltimore: The Williams & Wilkins Co. 1943.

**A MANUAL OF PULMONARY TUBERCULOSIS, AN ATLAS OF TUBERCULOUS ROENTGENOLOGY.** By David O. N. Lloyd, M.D., F.A.C.P. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1943.

**PHYSIOLOGY IN AVIATION.** By Chalmers L. Gessmiller, B.S., M.D. Springfield, Ill. and Baltimore, Md.: Charles C. Thomas, 1943.

